10774498

=> LOGOFF
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	261.75	428.90

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-35.25	-35.25

STN INTERNATIONAL LOGOFF AT 18:12:32 ON 10 DEC 2006

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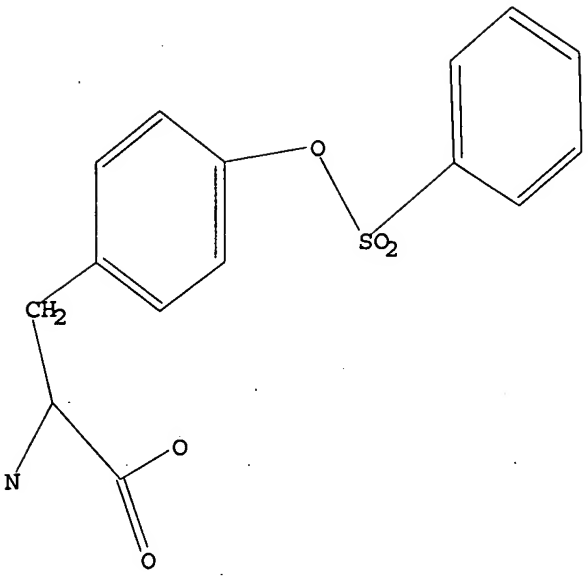

Structure attributes must be viewed using STN Express query preparation.

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=> S L1
SAMPLE SEARCH INITIATED 18:04:41 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       44 TO ITERATE

100.0% PROCESSED       44 ITERATIONS                                 7 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          483 TO     1277
PROJECTED ANSWERS:               7 TO      298

L2             7 SEA SSS SAM L1

=> S L1 FULL
FULL SEARCH INITIATED 18:04:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      753 TO ITERATE

100.0% PROCESSED      753 ITERATIONS                                78 ANSWERS
SEARCH TIME: 00.00.01

L3            78 SEA SSS FUL L1

=> FILE CAPLUS
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     166.94     167.15

FILE 'CAPLUS' ENTERED AT 18:04:53 ON 10 DEC 2006
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            20 SULFONICS
         78240 SULFONIC
                 (SULFONIC OR SULFONICS)
L8            0 L4 AND SULFONIC

=> D L4 IBIB ABS HITSTR TOT
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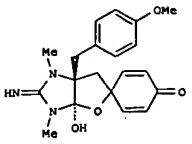
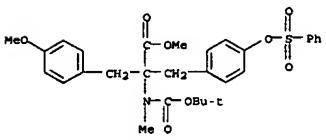
SAEED

L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:398311 CAPLUS
DOCUMENT NUMBER: 145:83561
TITLE: Synthetic studies toward spiroleucettadine
AUTHOR(S): Chang, Jonah J.; Chan, Bryan; Ciufolini, Marco A.
CORPORATE SOURCE: Department of Chemistry, University of British Columbia, Vancouver, BC, V6T 1Z1, Can.
SOURCE: Tetrahedron Letters (2006), 47(21), 3599-3601
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:83561
GI



I

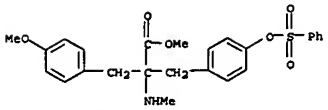
AB Synthetic hydroxydienone precursors to spiroleucettadine (I), and to an isomer thereof, resist cyclization to the orthoamide-type functionality present in the proposed structure of the natural product.
IT 894094-67-8P 894094-68-9P 894094-69-0P
894094-70-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthetic studies toward spiroleucettadine)
RN 894094-67-8 CAPLUS
CN Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-N,O-dimethyl-α-[[4-[(phenylsulfonyl)oxy]phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



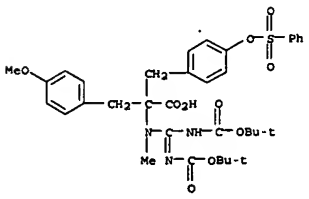
RN 894094-68-9 CAPLUS
CN Tyrosine, N,O-dimethyl-α-[[4-[(phenylsulfonyl)oxy]phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

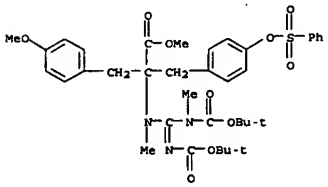
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 894094-69-0 CAPLUS
CN Tyrosine, N-[[[(1,1-dimethylethoxy)carbonyl]amino][[(1,1-dimethylethoxy)carbonyl]imino]methyl]-N,O-dimethyl-α-[[4-[(phenylsulfonyl)oxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

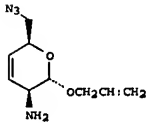


RN 894094-70-3 CAPLUS
CN Tyrosine, N-[[[(1,1-dimethylethoxy)carbonyl]imino][[(1,1-dimethylethoxy)carbonyl]methylamino]methyl]-N,O-dimethyl-α-[[4-[(phenylsulfonyl)oxy]phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

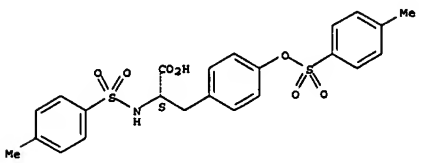
L4 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1155983 CAPLUS
DOCUMENT NUMBER: 142:240700
TITLE: The Overman rearrangement in carbohydrate chemistry: stereoselective synthesis of functionalized 3-amino-3,6-dihydro-2H-pyrans and incorporation in peptide derivatives
AUTHOR(S): Montero, Ana; Mann, Enrique; Herradon, Bernardo
CORPORATE SOURCE: C.S.I.C., Instituto de Quimica Organica General, Madrid, 28006, Spain
SOURCE: Tetrahedron Letters (2005), 46(3), 401-405
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:240700
GI



I

AB A stereocontrolled synthesis of unsatd. sugar I bearing two amino groups (one of them masked as an azide), using an Overman rearrangement as key step, is described. This scaffold is used to prepare two peptides having aromatic fragments, which have shown activity as calpain inhibitors.
IT 13504-90-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective synthesis of aminodihydropyran peptide derivs. as calpain inhibitors)
RN 13504-90-0 CAPLUS
CN L-Tyrosine, N-[(4-methylphenyl)sulfonyl]-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

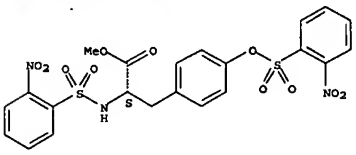


REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS

L4 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:973211 CAPLUS
DOCUMENT NUMBER: 140:146434
TITLE: Specific solvation as a tool for the N-chemoselective arylsulfonylation of tyrosine and (4-hydroxyphenyl)glycine methyl esters
AUTHOR(S): Penso, Michele; Albanese, Domenico; Landini, Dario; Lupi, Vittoria; Tricarico, Giovanni
CORPORATE SOURCE: CNR - Istituto di Scienze e Tecnologie Molecolari, Milan, 20133, Italy
SOURCE: European Journal of Organic Chemistry (2003), (23), 4513-4517
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:146434
AB The Me esters of L-tyrosine and D-(4-hydroxyphenyl)glycine were directly transformed into the corresponding 2-arylsulfonamido esters with arylsulfonyl chlorides, without protecting the phenolic hydroxy group. The reaction is conducted in a THF/DMF (8:1) mixture as solvent, and using lyophilized solid sodium carbonate as base. The N-arylsulfonylation takes place with good yields (62-85%) in a chemoselective fashion, without racemization of the stereogenic carbon centers. The DMF (2.6 mol/mol amino ester) specifically solvates the oxygen atom of the formed N,O-dianion, reducing its nucleophilicity and dramatically increasing the chemoselectivity of the N-substitution. In contrast, in the absence of a highly coordinating additive, the phenoxide anion competes unfavorably with the 2-amino group for the nucleophilic attack, and the N,O-disulfonyl esters are produced with relevant yields.
IT 652972-84-4P 652972-86-6P 652972-89-9P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of arylsulfonamido esters by arylsulfonylation of tyrosine and hydroxyphenylglycine Me esters with arylsulfonyl chlorides using specific solvation as tool)
RN 652972-84-4 CAPLUS
CN L-Tyrosine, N-[(2-nitrophenyl)sulfonyl]-, methyl ester, 2-nitrobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

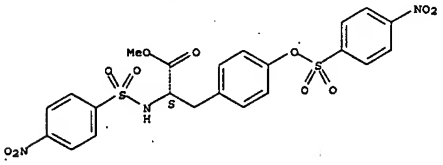
Absolute stereochemistry. Rotation (-).



L4 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

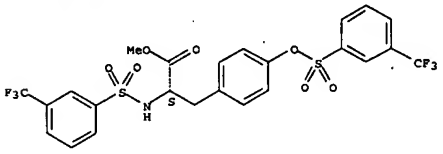
RN 652972-86-6 CAPLUS
CN L-Tyrosine, N-[(4-nitrophenyl)sulfonyl]-, methyl ester, 4-nitrobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 652972-89-9 CAPLUS
CN L-Tyrosine, N-[[3-(trifluoromethyl)phenyl]sulfonyl]-, methyl ester, 3-(trifluoromethyl)benzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



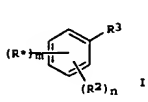
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:719441 CAPLUS
DOCUMENT NUMBER: 139:245761
TITLE: Process for preparation of biaryl compounds
INVENTOR(S): Ueda, Hiroshi; Kurimoto, Isao
PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Japan
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074478	A1	20030912	WO 2003-JP2460	20030304
W: US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
JP 2003327573	A2	20031119	JP 2003-45539	20030224
EP 1346971	A1	20030924	EP 2003-251300	20030304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004024229	A1	20040205	US 2003-377710	20030304
US 7091373	B2	20060815		
EP 1481967	A1	20041201	EP 2003-743573	20030304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
JP 2003342250	A2	20031203	JP 2003-67820	20030313
JP 2003342251	A2	20031203	JP 2003-67821	20030313
US 2004158093	A1	20040812	US 2004-774498	20040210
PRIORITY APPLN. INFO.:			JP 2002-58624 A	20020305
			JP 2002-73833 A	20020318
			WO 2003-JP2460 W	20030304

OTHER SOURCE(S): MARPAT 139:245761
GI

L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



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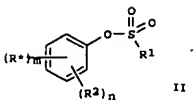
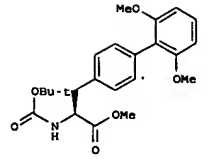


II



III

AB This invention pertains to a method for producing optically active biaryl compds. with general formula of I [wherein R3 = independently F, CN, NO2, OH, alkoxy, aryloxy, alkylthio, arylthio, CHO, alkylcarbonyl, arylcarbonyl, CO2H, alkoxycarbonyl, aryloxycarbonyl, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, amino, carbamoyl, or SO2NH2; R* = independently a chiral substituent, etc.; m = 1-5; n = 0-4; R3 = (un)substituted (hetero)aryl], which comprise reacting II [wherein R1 = (un)substituted alkyl or aryl; with exclusions] with R3BQ1Q2 [wherein Q1 and Q2 = independently OH or alkoxy; or Q1 and Q2 together form an (un)substituted alkylenedioxy or 1,2-phenylenedioxy]. For example, L-N-(tert-butoxycarbonyl)-O-(p-toluenesulfonyl)tyrosine Me ester (preparation given) was reacted with 2,6-dimethoxyphenylboronic acid in 1,4-dioxane in the presence of Cs2CO3, (C6H12)3P, and bis(1,5-cyclooctadiene)nickel to give III (100%) with 99.8% e.e. This invention provides a method to make biaryl compds. from inexpensive starting materials in high yield.

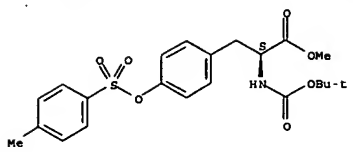
IT 596094-12-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of biaryl compds. by coupling reaction)

RN 596094-12-1 CAPLUS

CN L-Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-, methyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

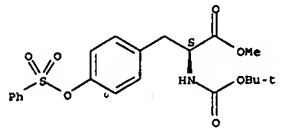


IT 596094-13-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of biaryl compds. by coupling reaction)

RN 596094-13-2 CAPLUS

CN L-Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-, methyl ester, benzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:408456 CAPLUS
DOCUMENT NUMBER: 139:254260
TITLE: 1-Prolinoyl chiral picket iron porphyrins evaluated for the enantioselective epoxidation of alkenes
AUTHOR(S): Boitrel, Bernard; Baveux-Chambenoit, Valerie
CORPORATE SOURCE: Laboratoire Organometalliques et Catalyse: Chimie et Electrochimie Moleculaire (CNRS UMR 6509), Institut de Chimie de Rennes, Campus de Beaulieu, Universite de Rennes 1, Rennes, 35042, Fr.
SOURCE: New Journal of Chemistry (2003), 27(6), 942-947
CODEN: NJCHE5; ISSN: 1144-0546
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:254260

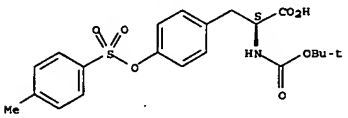
AB Four atropisomers of an 1-prolinoyl picket porphyrin were synthesized from tetra-o-aminophenyl porphyrin (TAPP) and were evaluated as alkene epoxidn. catalysts after incorporation of iron in the porphyrin core. In the case of the αααα atropisomer bearing the four amino groups on the same side, a bulky base was employed in order to suppress the eventual reaction on the non-functionalized side of the porphyrin. The resulting enantioselectivities were compared with either other chiral motifs or with the corresponding strapped porphyrins. The enantioselectivities obtained with picket porphyrins are as high as those for strapped porphyrins, and in some cases, even higher.

IT 597544-71-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(ligand synthesis; L-prolinoyl chiral picket iron porphyrins evaluated for the enantioselective epoxidn. of alkenes)

RN 597544-71-3 CAPLUS

CN L-Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

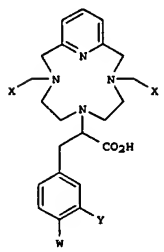
Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:291067 CAPLUS
DOCUMENT NUMBER: 139:142746
TITLE: Designing novel contrast agents for magnetic resonance imaging. Synthesis and relaxometric characterization of three gadolinium(III) complexes based on functionalized pyridine-containing macrocyclic ligands
AUTHOR(S): Aime, Silvio; Gianolio, Eliana; Corpillo, Davide; Cavallotti, Camilla; Palmisano, Giovanni; Sisti, Massimo; Giovenzana, Giovanni B.; Pagliarin, Roberto
CORPORATE SOURCE: Dip. di Chim., I. F. M.., Univ. degli Studi di Torino, Turin, I-10125, Italy
SOURCE: Helvetica Chimica Acta (2003), 86(3), 615-632
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:142746
GI

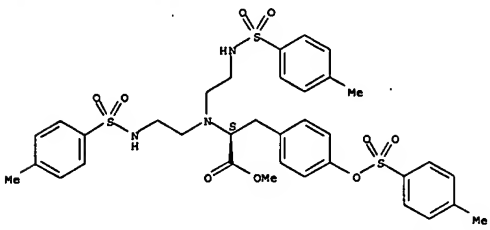


I

AB Three novel pyridine-containing 12-membered macrocyclic ligands (I: 1, X = COOH, W = Y = H; 2, X = PO3H2, W = Y = H; 3, X = Y = COOH, W = OCH2COOH) were synthesized. The coordinating arms are represented by three acetate moieties in 1 and 3 and by one acetate and two phosphonate moieties in 2. In all three ligands, the acetate arm in the distal position is substituted, with a benzyl group in 1 and 2 and with an arylmethyl moiety in 3. The relaxivities rlp (20 MHz, 25°) of GdIII complexes are: Gd·1, rlp = 8.3 mM-1 s-1; Gd·2, rlp = 8.1 mM-1 s-1; Gd·3, rlp = 10.5 mM-1 s-1. 1H-NMRD and 17O-NMR T2 data show that Gd·1 and Gd·3 contain two H2O mols. in the inner sphere, whereas the presence of two phosphonate arms allows the coordination of only one H2O mol. in Gd·2. The exchange lifetime of coordinated H2O in the three complexes is similar in spite of the difference in the coordination number of the GdIII ion (i.e., 9 in Gd·1 and Gd·3, and 8 in Gd·2). 1H-Relaxometric measurements at different pH and

L4 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
in the presence of lactate and oxalate were carried out to get some insight into the formation of ternary complexes from Gd·1 and Gd·3. Finally, binding to human-serum albumin (HSA) of Gd·1 and Gd·2, though weak, yields limited relaxivity enhancements, likely as a consequence of effects on the hydration sphere caused by donor
atoms on the surface of the protein.
IT 566916-75-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of gadolinium(III) complexes of functionalized pyridine-containing
macrocyclic ligands)
RN 566916-75-4 CAPLUS
CN L-Tyrosine, N,N-bis[2-[[(4-methylphenyl)sulfonyl]amino]ethyl]-, methyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



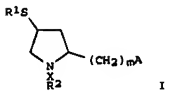
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:72037 CAPLUS
DOCUMENT NUMBER: 136:134667
TITLE: Preparation of mercaptopyrrolidinecarboxamides related
compounds as inhibitors of endothelin-converting enzyme
INVENTOR(S): Aebi, Johannes; Blum, Denise; Bur, Daniel; Chucholowski, Alexander; Dehmlow, Henriette; Kitas, Eric Argirios; Loeffler, Bernd Michael; Obst, Ulrike; Wallbaum, Sabine
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006222	A1	20020124	WO 2001-EP7950	20010710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2414311	AA	20020124	CA 2001-2414311	20010710
EP 1303485	A1	20030423	EP 2001-949485	20010710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012580	A	20030617	BR 2001-12580	20010710
JP 2004504297	T2	20040212	JP 2002-512128	20010710
CN 1620433	A	20050525	CN 2001-813023	20010710
US 2002049243	A1	20020425	US 2001-907135	20010717
US 6541638	B2	20030401		
ZA 2003000167	A	20040407	ZA 2003-167	20030107
PRIORITY APPLN. INFO.:			EP 2000-114947 A	20000719
			WO 2001-EP7950 W	20010710

OTHER SOURCE(S): MARPAT 136:134667
GI

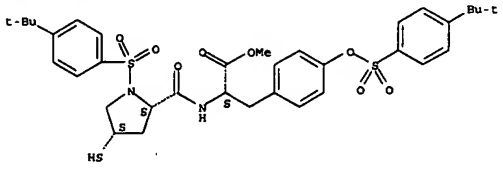
L4 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I

AB Title compds. [I; R1 = H, alkylcarbonyl, arylcarbonyl; R2 = alkyl, alkylcycloalkyl, cycloalkyl, haloalkyl, carboxyalkyl, aryl, alkynyl, aryloxyalkyl, heterocyclyl, etc.; A = COR3, CH(OH)R4, CONR5R6; R3, R4 = alkyl, aryl, arylalkynyl, aralkyl, arylalkenyl; R5 = H, alkyl, cycloalkyl,
cycloalkylalkyl, carboxyalkyl, aralkyl; R6 = alkyl, alkylcarbonylalkyl, cyanoalkyl, hydroxyalkyl, aminocarbonylalkyl, aryl, etc.; m = 0-2; X = SO2, CO, CO2, SO2NH, CONR13; R13 = H, alkyl, aryl, carboxyalkyl], and dimers thereof, were prepared Thus,
(2S,4R)-[[4-(4-methoxybenzylsulfanyl)-1-(naphthalene-2-sulfonyl)pyrrolidine-2-carbonyl]methylamino]acetic acid (preparation given) in CH2Cl2 were treated with NMM, HOBT in CH2Cl2, EDCI in
CH2Cl2, and o-toluidine in CH2Cl2; the solution was shaken overnight to give
a residue which was treated with Et3SiH in CF3CO2H at 80° for 1 h to give (2S,4R)-4-mercapto-1-(naphthalene-2-sulfonyl)pyrrolidine-2-carboxylic acid methyl(o-tolylcarbamoylmethyl)amide. I inhibited endothelin converting enzyme with IC50 = 5-1000 nM.
IT 393156-86-0P 393156-90-6P 393156-92-8P
393156-94-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of mercaptopyrrolidinecarboxamides as inhibitors of endothelin-converting enzyme)
RN 393156-86-0 CAPLUS
CN L-Tyrosine, (4S)-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4-mercapto-L-prolyl-, methyl ester, 2-[4-(1,1-dimethylethyl)benzenesulfonate] (9CI) (CA INDEX NAME)

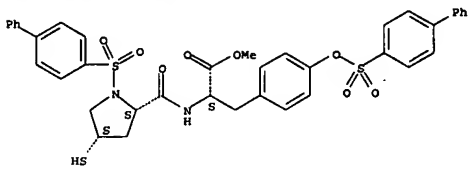
Absolute stereochemistry.



RN 393156-90-6 CAPLUS

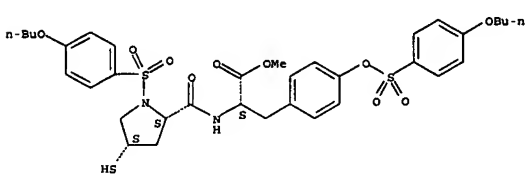
L4 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN L-Tyrosine, (4S)-1-([1,1'-biphenyl]-4-ylsulfonyl)-4-mercapto-L-prolyl-, methyl ester, 2-([1,1'-biphenyl]-4-sulfonate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393156-92-8 CAPLUS
CN L-Tyrosine, (4S)-1-[(4-butoxyphenyl)sulfonyl]-4-mercapto-L-prolyl-, methyl
ester, 2-(4-butoxybenzenesulfonate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393156-94-0 CAPLUS
CN L-Tyrosine, (4S)-1-[(3,4-dimethoxyphenyl)sulfonyl]-4-mercapto-L-prolyl-, methyl ester, 2-(3,4-dimethoxybenzenesulfonate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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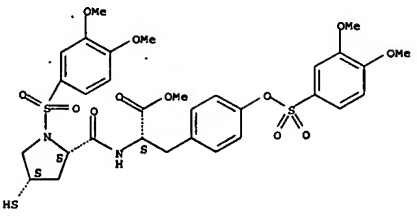
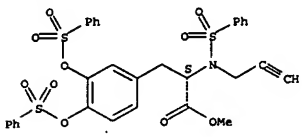
L4 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:126201 CAPLUS
DOCUMENT NUMBER: 134:266170
TITLE: Palladium catalyzed tandem cyclization-anion capture. Part 7: synthesis of derivatives of α-amino esters, nitrogen heterocycles, and β-aryl/heteroaryl ethylamines via in situ generated vinylstannanes
AUTHOR(S): Casaschi, Adele; Grigg, Ronald; Sansano, J. M.
CORPORATE SOURCE: Molecular Innovation, Diversity and Automated Synthesis (MIDAS) Centre, Leeds University, Leeds, LS2 9JT, UK
SOURCE: Tetrahedron (2001), 57(3), 607-615
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:266170
AB Palladium catalyzed in situ hydrostannylation of terminal alkynes containing a β-N atom affords mainly α-vinylstannanes which serve as anion capture agents in palladium catalyzed cyclization-anion capture processes leading to derivs. of α-amino esters, nitrogen heterocycles, and β-aryl/heteroaryl ethylamines in good yield.
IT 331731-78-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(palladium catalyzed cascade hydrostannylation-cyclization-anion capture)
RN 331731-78-3 CAPLUS
CN L-Tyrosine, N-(phenylsulfonyl)-3-[(phenylsulfonyl)oxy]-N-2-propynyl-, methyl ester, benzenesulfonate (ester) (9CI) (CA INDEX NAME)

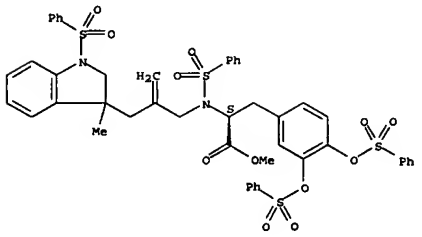
Absolute stereochemistry. Rotation (-).



IT 331731-89-6P 331731-90-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(palladium catalyzed cascade hydrostannylation-cyclization-anion capture)
RN 331731-89-6 CAPLUS
CN L-Tyrosine, N-[2-[[2,3-dihydro-3-methyl-1-(phenylsulfonyl)-1H-indol-3-yl]methyl]-2-propenyl]-N-(phenylsulfonyl)-3-[(phenylsulfonyl)oxy]-, methyl
ester, benzenesulfonate (ester) (9CI) (CA INDEX NAME)

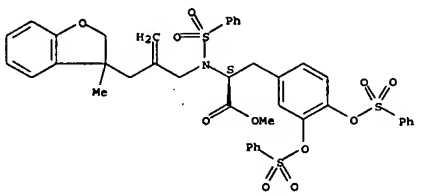
L4 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



RN 331731-90-9 CAPLUS
CN L-Tyrosine, N-[2-[(2,3-dihydro-3-methyl-3-benzofuranyl)methyl]-2-propenyl]-N-(phenylsulfonyl)-3-[(phenylsulfonyl)oxy]-, methyl ester, benzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

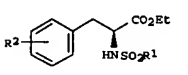


REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:708597 CAPLUS
DOCUMENT NUMBER: 131:310836
TITLE: Preparation of phenylalanine sulfonamide derivatives as CCR-3 receptor antagonists
INVENTOR(S): Dhanak, Dashyant
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955324	A1	19991104	WO 1999-US9182	19990427
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2329777	AA	19991104	CA 1999-2329777	19990427
EP 1076557	A1	20010221	EP 1999-920102	19990427
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2002512957	T2	20020508	JP 2000-545523	19990427
PRIORITY APPLN. INFO.:			US 1998-83228P P	19980427
			WO 1999-US9182 W	19990427

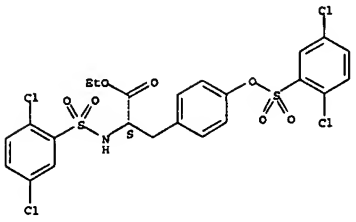
OTHER SOURCE(S): MARPAT 131:310836
GI



AB The title compds. I [R1 = alkyl, aryl, heteroaryl; R2 = 4-OH, 4-(2,5-Cl2C6H3)O, 4-(2,4-F2C6H3)O], CCR-3 receptor antagonists (no data), were prepared (S)-Et 2-(4-methylbenzenesulfonylamino)-3-(4-hydroxyphenyl)propionate was prepared from L-tyrosine Et ester and TsCl.
IT 247247-83-2P 247247-84-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylalanine sulfonamide derivs. as CCR-3 receptor antagonists)
RN 247247-83-2 CAPLUS
CN L-Tyrosine, N-[(2,5-dichlorophenyl)sulfonyl]-, ethyl ester, 2,5-dichlorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

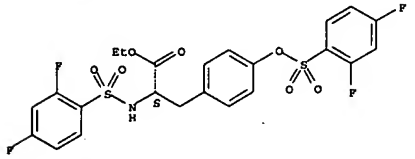
Absolute stereochemistry.

L4 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 247247-84-3 CAPLUS
CN L-Tyrosine, N-[(2,4-difluorophenyl)sulfonyl]-, ethyl ester, 2,4-difluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

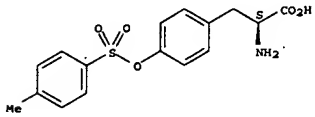
L4 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:428026 CAPLUS
DOCUMENT NUMBER: 131:41799
TITLE: Method and reagent for detecting microorganisms displaying deaminase activity
INVENTOR(S): Armstrong, Lyle; James, Arthur; Orenga, Sylvain
PATENT ASSIGNEE(S): Bio Merieux S. A., Fr.
SOURCE: Fr. Demande, 30 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2770538	A1	19990507	FR 1997-14191	19971106
FR 2770538	B1	20001013		
CA 2309297	AA	19990520	CA 1998-2309297	19981106
WO 9924604	A1	19990520	WO 1998-FR2380	19981106
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9911606	A1	19990531	AU 1999-11606	19981106
EP 1029073	A1	20000823	EP 1998-954534	19981106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001521764	T2	20011113	JP 2000-519597	19981106
US 6733986	B1	20040511	US 2000-530518	20000525
PRIORITY APPLN. INFO.:			FR 1997-14191 A	19971106
			WO 1998-FR2380 W	19981106

OTHER SOURCE(S): MARPAT 131:41799
AB To detect microorganisms containing a deaminase, such as Proteus, an amino acid derivative Xn-R-CH2CH(NH2)CO2H (I; X = a group such as naphthalenesulfonyl, tosylsulfonyl, and mesitylenesulfonyl; n = 1,2,3; R = cyclic/heterocyclic side chain) is added to the culture medium. Presence of the deaminase-producing microbe is evidenced by formation of a colored product. I is synthesized by formylation of the amino acid, reaction of a salt of X with formylated amino acid, and deformylation of the product. Syntheses of several I were presented. A culture medium containing brain-heart extract, bio-Soyase, Tris buffer, KH2PO4, iron ammonium citrate, 4-O-toluenesulfonyl-L-tyrosine (a compound of the invention), 4-bromo-4-chloro-3-indolyl-β-D-glucoside, 6-chloro-3-indolyl-β-D-glucuronide, and methyl-βD-glucuronide, pH 7.2, was used to differentiate four types of urinary bacteria. Morganella morganii, P.

L4 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
mirabilis and P. vulgaris were detected with the 4-O-toluenesulfonyl-L-tyrosine.
IT 13504-89-7P
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(method and reagent for detecting microorganisms displaying deaminase activity)
RN 13504-89-7 CAPLUS
CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

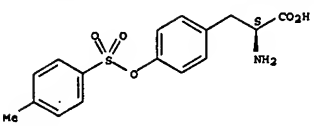
Absolute stereochemistry.



L4 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:327924 CAPLUS
DOCUMENT NUMBER: 131:141312
TITLE: Structure-based discovery and in-parallel optimization of novel competitive inhibitors of thymidylate synthase
AUTHOR(S): Tondi, Donatella; Slomczynska, Ursula; Costi, M. Paola; Watterson, D. Martin; Ghelli, Stefano; Shoichet, Brian K.
CORPORATE SOURCE: Department of Molecular Pharmacology and Biological Chemistry, Northwestern University, Chicago, IL, 60611-3008, USA
SOURCE: Chemistry & Biology (1999), 6(5), 319-331
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Current Biology Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The substrate sites of enzymes are attractive targets for structure-based inhibitor design. Two difficulties hinder efforts to discover and elaborate new (nonsubstrate-like) inhibitors for these sites. First, novel inhibitors often bind at nonsubstrate sites. Second, a novel scaffold introduces chemical that is frequently unfamiliar, making synthetic elaboration challenging. In an effort to discover and elaborate a novel scaffold for a substrate site, we combined structure-based screening with in-parallel synthetic elaboration. These techniques were used to find new inhibitors that bound to the folate site of Lactobacillus casei thymidylate synthase (LcTS), an enzyme that is a potential target for proliferative diseases, and is highly studied. The available chems. directory was screened, using a mol.-docking computer program, for mols. that complemented the three-dimensional structure of this site. Five high-ranking compds. were selected for testing. Activity and docking studies led to a derivative of one of these, dansyltyrosine (Ki 65 μM). Using solid-phase in-parallel techniques 33 derivs. of this lead were synthesized and tested. These analogs are dissimilar to the substrate but bind competitively with it. The most active analog had a Ki of 1.3 μM. The tighter binding inhibitors were also the most specific for LcTS vs. related enzymes. TS can recognize inhibitors that are dissimilar to, but that bind competitively with, the folate substrate. Combining structure-based discovery with in-parallel synthetic techniques allowed the rapid elaboration of this series of compds. More automated versions of this approach can be envisaged.
IT 13504-89-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-based discovery and in-parallel optimization of novel competitive inhibitors of thymidylate synthase)
RN 13504-89-7 CAPLUS
CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:795039 CAPLUS
DOCUMENT NUMBER: 130:52733
TITLE: Preparation of tyrosine derivatives as antiinflammatory agents
INVENTOR(S): Head, John Clifford; Archibald, Sarah Catherine; Warrellow, Graham John
PATENT ASSIGNEE(S): Celltech Therapeutics Limited, UK
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854207	A1	19981203	WO 1998-GB1580	19980529
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876674	A1	19981230	AU 1998-76674	19980529
EP 984981	A1	20000315	EP 1998-924481	19980529
EP 984981	B1	20031217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6093696	A	20000725	US 1998-86421	19980529
JP 2002501518	T2	20020115	JP 1999-500393	19980529
AT 256699	E	20040115	AT 1998-924481	19980529

PRIORITY APPLN. INFO.: GB 1997-11143 A 19970530
GB 1997-22674 A 19971027
WO 1998-GB1580 W 19980529

OTHER SOURCE(S): MARPAT 130:52733
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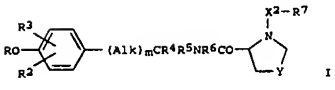
L4 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



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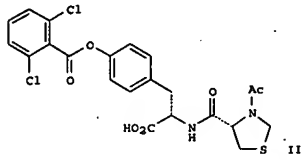


II

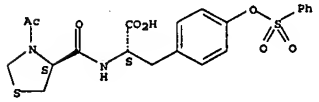
AB Tyrosine derivs. I (R = R1X1, (Hal1)3CSO2; R1 = optionally substituted alkyl or aromatic group; R2, R3 = independently H, halo, alkyl, alkoxy, OH, NO2; R4 = H, Me; R5 = (CH2)pCO2R8; R6 = H, alkyl; R7 = optionally substituted alkyl group, aryl, aralkyl; R8 = H, alkyl; Alk = alkylene chain; Hal1 = F, Cl; X1 = bond, (CH2)n, CO, CH2CO, NHCO, CH2NHCO, SO2; X2 = CO, CO2, CONH, SO2; Y = S, S(O)q; m = 0, 1; n = 1, 2; p = 0, 1; q = 1, 2] and the salts, solvates and hydrates thereof, are described. The compds. are able to inhibit the binding of α4 integrins to their ligands and are of use in the prophylaxis and treatment of immune or inflammatory disorders. Thus, coupling of N-acetyl-D-thioproline with L-tyrosine tert-Bu ester, followed by O-acylation with 2,6-dichlorobenzoyl chloride and acidic deesterification, gave desired tyrosine derivative II. II and related thioprolyltyrosine derivs. were tested for inhibition of α4 integrin-dependent cell adhesion, and generally have IC50 values of ≤1 μM in α4β1 and α4β7 assays, and IC50 values of ≥ 50 μM in assays of other integrins.

IT 217479-28-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tyrosine derivs. as antiinflammatory agents)

RN 217479-28-2 CAPLUS
CN L-Tyrosine, N-[[(4S)-3-acetyl-4-thiazolidinyl]carbonyl]-, benzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

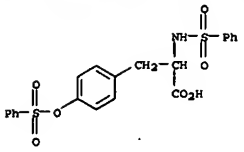
L4 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:712947 CAPLUS
DOCUMENT NUMBER: 126:30933
TITLE: Synthesis and Protein Kinase C Inhibitory Activities of Acyclic Balanol Analogs That Are Highly Selective for Protein Kinase C over Protein Kinase A
AUTHOR(S): Defauw, Jean M.; Murphy, Marcia M.; Jagdmann, G. Erik, Jr.; Hu, Hong; Lampe, John W.; Hollinshead, Sean P.; Mitchell, Thomas J.; Crane, Heidi M.; Heerding, Julia M.; et al.
CORPORATE SOURCE: Division of Eli Lilly and Company, Sphinx Pharmaceuticals, Durham, NC, 27707, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(26), 5215-5227
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of balanol analogs in which the perhydroazepine ring and the p-hydroxybenzamide moiety were combined into an acyclic linked unit have been prepared and evaluated for their inhibitory properties against the serine/threonine kinase PKC. Several low-micromolar to low-nanomolar inhibitors of the α, βI, βII, γ, δ, ε, and η PKC isoenzymes were prepared In general, these acyclic balanol analogs were found to be highly selective for PKC over the serine/threonine kinase PKA. The type and number of atoms linking the benzophenone ester to the p-hydroxyphenyl group necessary for optimal PKC inhibition were investigated. The most potent compds. contained a three-carbon linker in which the carboxamide moiety of balanol had been replaced by a methylene group. The effect of placing substituents on the three-carbon chain was also investigated. The preferred compds. contained either a 2-benzenesulfonamido or a 1-Me substituent. The preferred compds. were tested against a panel of serine/threonine kinases and found to be highly selective for PKC. The effect of making the analogs more rigid by making the three-carbon chain part of a five-membered ring, but with retention of the methylene replacement for the carboxamide moiety, led to potent PKC inhibitors including an anti-substituted pyrrolidine analog and an anti-substituted cyclopentane analog. The anti cyclopentane analog was a low-micromolar inhibitor of the PMA-induced superoxide burst in neutrophils, and its carboxylic ester was a high-nanomolar inhibitor of neutrophils. Esterification of these potent PKC inhibitors turned them into low-micromolar inhibitors of neutrophils.

IT 184592-39-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and protein kinase C inhibitory activities of acyclic balanol analogs)

RN 184592-39-0 CAPLUS
CN Tyrosine, N,O-bis(phenylsulfonyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:267995 CAPLUS
DOCUMENT NUMBER: 124:305630
TITLE: Dimeric DTPA derivatives and their metal complexes, pharmaceutical media containing these complexes, their use in der diagnostics and therapy and process for the preparation of the complexes and the media
INVENTOR(S): Krause, Werner; Maier, Franz-Karl; Bauer, Michael; Press, Wolf-Ruediger; Schuhmann-Giampieri, Gabriele; Platzek, Johannes; Schmitt-Willich, Heribert
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 25 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4428874	A1	19960222	DE 1994-4428874	19940808
US 5695737	A	19971209	US 1995-476117	19950607
CA 2197074	AA	19960222	CA 1995-2197074	19950808
WO 9605167	A1	19960222	WO 1995-EP3142	19950808
W: AU, BY, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, RU, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9533433	A1	19960307	AU 1995-33433	19950808
AU 695878	B2	19980827		
ZA 9506650	A	19960319	ZA 1995-6650	19950808
EP 775104	A1	19970528	EP 1995-929815	19950808
EP 775104	B1	19990506		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1156442	A	19970806	CN 1995-194571	19950808
JP 10503777	T2	19980407	JP 1995-506999	19950808
HU 77532	A2	19980528	HU 1997-370	19950808
AT 179696	E	19990515	AT 1995-929815	19950808
ES 2134487	T3	19991001	ES 1995-929815	19950808
FI 9700535	A	19970207	FI 1997-535	19970207
NO 9700602	A	19970210	NO 1997-602	19970210

PRIORITY APPLN. INFO.: DE 1994-4428874 A 19940808
WO 1995-EP3142 W 19950808

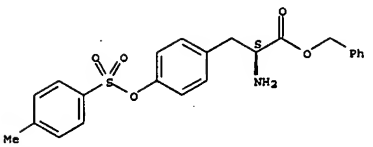
AB Dimeric diethylenetriaminepentaacetic acid derivs. and their metal complexes (Z = 21-32, 37-39, 42-51, and 57-83) were prepared Contrast agents using these compds. were prepared for use in nuclear medicine.

IT 102559-49-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of metal complexes with dimeric diethylenetriaminepentaacetic acid derivs. as contrast agent for nuclear medicine)

RN 102559-49-9 CAPLUS
CN L-Tyrosine, phenylmethyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



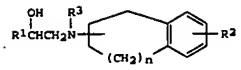
L4 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:106568 CAPLUS
DOCUMENT NUMBER: 120:106568
TITLE: (Ethanolamino)benzocycloalkane derivatives having sympathomimetic and anti-pollakiuria activities
INVENTOR(S): Shiokawa, Youichi; Nagano, Masanobu; Taniguchi, Kiyoshi; Take, Kazuhiko; Kato, Takeshi; Tsubaki, Kazunori
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9315041	A1	19930805	WO 1993-JP113	19930201
W: AU, CA, HU, JP, KR, RU, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9300591	A	19931018	ZA 1993-591	19930127
IL 104567	A1	19970318	IL 1993-104567	19930131
AU 9333679	A1	19930901	AU 1993-33679	19930201
AU 666162	B2	19960201		
EP 583485	A1	19940223	EP 1993-914517	19930201
EP 583485	B1	19970813		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 65351	A2	19940502	HU 1993-3112	19930201
HU 218941	B	20010129		
JP 06506955	T2	19940804	JP 1993-513097	19930201
JP 2819435	B2	19981030		
AT 156804	E	19970815	AT 1993-914517	19930201
ES 2105286	T3	19971016	ES 1993-914517	19930201
RU 2125983	C1	19990210	RU 1993-58393	19930201
JP 11092432	A2	19990406	JP 1998-130167	19930201
JP 3282799	B2	20020520		
CN 1084846	A	19940406	CN 1993-102681	19930202
CN 1063430	B	20010321		
US 5387710	A	19950207	US 1993-117163	19930917

PRIORITY APPLN. INFO.: GB 1992-2236 A 19920203
GB 1992-17991 A 19920824
JP 1993-513097 A3 19930201
WO 1993-JP113 A 19930201

OTHER SOURCE(S): MARPAT 120:106568
GI

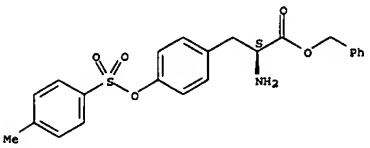
L4 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I

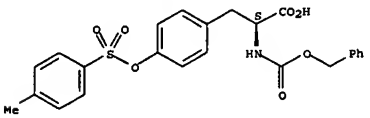
AB The title compds. I [R1 = (un)substituted aryl or heterocyclic group; R2 = H, halogen, NO2, HO, (un)substituted lower alkyl, (un)substituted lower alkenyl, (un)substituted lower alkoxy, (un)substituted NH2; R3 = H, a N-protective group, (un)substituted lower alkyl; n = 0-3; the heavy solid line represents a single or double bond, etc.], useful for the treatment of dysuria, spasm, or hyperanakinesia, are prepared Thus, 6-amino-3-ethoxycarbonylmethoxy-6,7,8,9-tetrahydro-5H-benzocycloheptene was refluxed with (R)-3-chlorostyrene oxide in PrOH, and the intermediate acidified with EtOAc containing HCl, producing a mixture of (1R,6'R)- and (1R,6'S)-2-[(3-ethoxycarbonylmethoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-6-yl)amino]-1-(3-chlorophenyl)ethanol hydrochoride (II), m.p. 114-119°. II demonstrated 50% inhibitory concentration against contractions of isolated rat distal colon of 6.8 x 10-10 M.
IT 102559-49-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction. of, in preparation of sympathomimetic and anti-pollakiuria activity compds.)
RN 102559-49-9 CAPLUS
CN L-Tyrosine, phenylmethyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



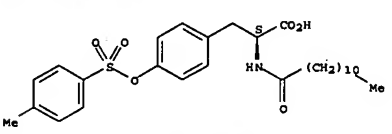
L4 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:234447 CAPLUS
DOCUMENT NUMBER: 118:234447
TITLE: Diastereoselective hydrogenation of monodehydro enkephalins controlled by chiral rhodium catalysts
AUTHOR(S): Hammadi, A.; Nuzillard, J. M.; Poulin, J. C.; Kagan, H. B.
CORPORATE SOURCE: Inst. Chim. Mol., Univ. Paris-Sud, Orsay, 91405, Fr.
SOURCE: Tetrahedron: Asymmetry (1992), 3(10), 1247-62
CODEN: TASYE3; ISSN: 0957-4166
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 118:234447
AB Protected dehydro leucine-enkephalins Z-Tyr(R)-Gly-Gly-ΔPhe-Leu-OMe [Z = PhCH2O2C, R = PhCH2, tosyl, ΔPhe = (Z)-dehydrophenylalanine] and Z-ΔTyr(R)-X-Gly-Phe-Leu-OMe [ΔTyr = (Z)-dehydrotyrosine, X = Ala, Gly, R = same] were prepared and hydrogenated in the presence of various chiral rhodium complexes to give protected leucine-enkephaline. Deprotection with Yb in liquid ammonia allows smooth deprotection of Z or tosyl groups on small amts. of peptides to give the leucine-enkephalins or their epimers. Strong stereocontrol could be achieved by suitable choice of the chiral catalyst. This method has good potential for stereospecific labeling of enkephalins and other small peptides.
IT 106111-10-8, N-Benzyloxycarbonyl-O-tosyltyrosine
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with glycine ester)
RN 106111-10-8 CAPLUS
CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:209578 CAPLUS
DOCUMENT NUMBER: 114:209578
TITLE: Synthesis of N-acyl amino acids and correlation of structure with surfactant properties of their sodium salts
AUTHOR(S): Bhaskar, S. Y.; Prasad, R. B. N.; Lakshminarayana, G.
CORPORATE SOURCE: Indian Inst. Chem. Technol., Hyderabad, 500007, India
SOURCE: Journal of the American Oil Chemists' Society (1990), 67(12), 1015-19
CODEN: JAOCA7; ISSN: 0003-021X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of structural variation in fatty acid and amino acid moieties on surfactant properties of Na salts of N-acyl condensates of amino acids was investigated. Pure N-acyl leucines and N-lauroyl condensates of different amino acids were synthesized and neutralized. Among the N-acyl leucinates, N-lauroyl leucinate exhibited optimum properties and compared well with Na lauryl aulfate (I). Among the salts of N-α-lauroylamino acids, N-α-lauroyl lysinate was comparable to I. Salts of N-α-lauroyl condensates of leucine, tryptophan, phenylalanine (II) and proline (III) showed good wetting ability; III also displayed high Ca ion tolerance. Salts of N-lauroyl tyrosine and II exhibited good foaming ability. N-Lauroyl aspartate showed inferior properties compared to I in spite of having an addnl. carboxylic group.
IT 133377-02-3P, O-Tosyl-N-lauroyl tyrosine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and detosylation of)
RN 133377-02-3 CAPLUS
CN L-Tyrosine, N-(1-oxododecyl)-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

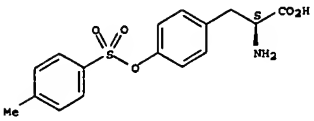
Absolute stereochemistry.



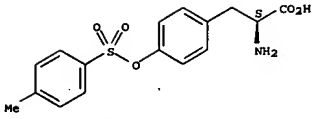
IT 13504-89-7, O-Tosyl tyrosine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation reaction of, with lauroyl chloride)
RN 13504-89-7 CAPLUS
CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

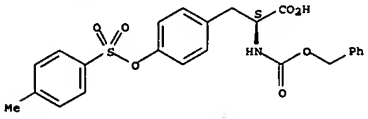


L4 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



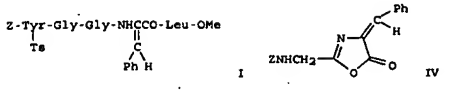
IT 106111-10-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with glycine Et ester)
RN 106111-10-8 CAPLUS
CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:50621 CAPLUS
DOCUMENT NUMBER: 106:50621
TITLE: Synthesis of a protected monodehydro Leu-enkephalin and its hydrogenation catalyzed by chiral rhodium complexes
AUTHOR(S): Nuzillard, J. M.; Poulin, J. C.; Kagan, H. B.
CORPORATE SOURCE: Lab. Synth. Asymetr., Univ. Paris-Sud, Orsay, 91405, Fr.
SOURCE: Tetrahedron Letters (1986), 27(26), 2993-6
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:50621
GI



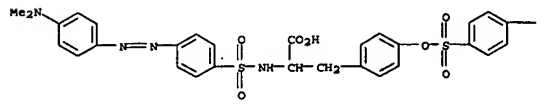
AB Protected monodehydro enkephalin analog I (Z = PhCH2O2C, Ts = tosyl) was prepared in 80% yield by coupling Z-Tyr(Ts)-Gly-OH (II) with H-Gly-ΔPhe-Leu-OMe.HBr (III) by DCC in the presence of Et3N. III was prepared by cyclizing Z-Gly-PhSer-OH (PhSer = β-phenylserine residue) with Ac2O, coupling the resulting oxazolone IV with H-Leu-OMe.HCl, and Z-deblocking the resulting Z-Gly-ΔPhe-Leu-OMe by HBr/HOAc. II was prepared from tyrosine and H-Gly-OEt.HCl by conventional solution methods. I underwent asym. hydrogenation over chiral rhodium catalyst in MeOH at 150° for 48 h; [Rh(dipamp)(COD)]+ BF4- gave a large excess of the S-configuration with a diastereoisomeric excess (de) of 93%, whereas RhCl(-)-bppm gave an excess of the R-configuration with a de of 68%.
IT 13504-89-7P, O-Tosyl-(S)-tyrosine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and benzyloxycarbonylation of)
RN 13504-89-7 CAPLUS
CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

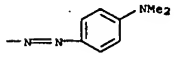
L4 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:479317 CAPLUS
DOCUMENT NUMBER: 105:79317
TITLE: Complete high-performance liquid chromatographic separation of 4-N,N-dimethylaminoazobenzene-4'-thiohydantoin and 4-dimethylaminoazobenzene-4'-sulfonyl chloride amino acids utilizing the same reversed-phase column at room temperature
AUTHOR(S): Stocchi, Vilberto; Cucchiarini, Luigi; Piccoli, Giovanni; Magnani, Mauro
CORPORATE SOURCE: Ist. Chim. Biol., Univ. Urbino, Urbino, Italy
SOURCE: Journal of Chromatography (1985), 349(1), 77-82
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reversed-phase high-performance liquid chromatog. methods for the complete separation of title amino acid derivs. on the same Supelcosil LC-18 column at room temperature are described. The procedures are simple and reproducible, and the systems are easily interconvertible. The use of a fixed-wavelength detector at 436 nm permits amino acid anal. at levels lower than 1 pmol with a stable baseline.
IT 103676-14-8
RL: PROC (Process)
(separation of, by reversed-phase high-performance liquid chromatog.)
RN 103676-14-8 CAPLUS
CN L-Tyrosine, N-[[4-[[4-(dimethylamino)phenyl]azo]phenyl]sulfonyl]-, 4-[[4-(dimethylamino)phenyl]azo]benzenesulfonate (ester) (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L4 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:501248 CAPLUS
DOCUMENT NUMBER: 103:101248
TITLE: The use of p-fluorobenzenesulfonyl chloride as a reagent for studies of proteins by fluorine nuclear magnetic resonance
AUTHOR(S): Liao, Ta Hsiu; Berlin, K. Darrell
CORPORATE SOURCE: Dep. Biochem., Oklahoma State Univ., Stillwater, OK, 74078, USA
SOURCE: Analytical Biochemistry (1985), 148(2), 365-75
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English

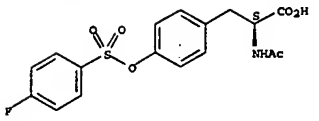
AB The reagent p-fluorobenzenesulfonyl chloride modifies the protein side chains of tyrosine, lysine, and histidine and the α-NH2 group. The p-fluorobenzenesulfonyl (Fbs-) group, identified by the 19F NMR signal, exhibits a different 19F chemical shift for each functional group modified.
The Fourier-transformed spectra of the Fbs- group displayed the expected 9-line multiplet in Fbs-amino acids and simple Fbs-peptides but not i n the Fbs-proteins, where the resolution was reduced. Lysozyme, RNase, DNase,
and chymotrypsin react with this reagent and each Fbs-protein exhibits a distinctive pattern of 19F NMR signals due to the label, suggesting that the reaction of the reagent varies with the reactivity of the side chains in a protein. The 3 major 19F signals of the unfolded Fbs-RNase in 8M urea are due to the Fbs label on the imidazolium, α-NH2, and ε-NH2 groups. Based upon results from amino acid and 19F NMR analyses of the tryptic-chymotryptic peptides of Fbs-RNase, portions of the imidazolium and ε-NH2 resonances were assigned to the Fbs-label on His-105 and Lys-41, resp., whereas the α-NH2 resonance was entirely due to the Fbs-label on the α-NH2 of Lys-1. Because Fbs-RNase has an unchanged, near-UV CD spectrum and because it retains .apprx.80% of the RNase activity, the conformation of Fbs-RNase is probably not altered from the folded conformation of the native enzyme. Upon unfolding in 8M urea or heating at 70°, Fbs-RNase gave a 19F NMR spectrum differing from that of the folded Fbs-RNase. In the presence
of uridylic acid, Lys-41 was the only residue protected from modification by the reagent, with a concomitant reduction of the ε-NH2 resonance, the RNase thus modified was fully active. Hence, 19F NMR anal. of proteins after reaction with p-fluorobenzenesulfonyl chloride, provided not only information about the protein conformation but also direct measurements of the modification status.

IT 97801-25-7 97801-39-3 97813-55-3
RL: PRP (Properties)
(NMR of)

RN 97801-25-7 CAPLUS
CN L-Tyrosine, N-acetyl-, 4-fluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

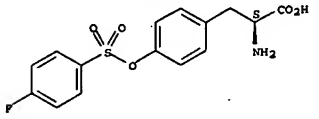
Absolute stereochemistry.

L4 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



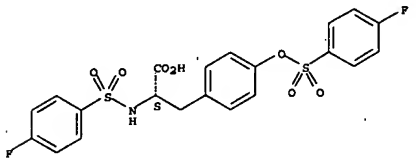
RN 97801-39-3 CAPLUS
CN L-Tyrosine, 4-fluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 97813-55-3 CAPLUS
CN L-Tyrosine, N-[(4-fluorophenyl)sulfonyl]-, 4-fluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



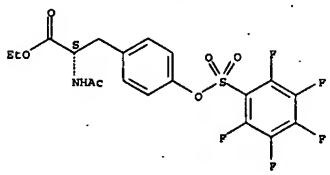
L4 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:566526 CAPLUS
DOCUMENT NUMBER: 101:166526
TITLE: Pentafluorobenzenesulfonyl chloride: a new electrophoric derivatizing reagent with application to
tyrosyl peptide determination by gas chromatography with electron capture detection
AUTHOR(S): Sentissi, Abdellah; Joppich, Markus; O'Connell, Kathleen; Nazareth, Albert; Giese, Roger W.
CORPORATE SOURCE: Dep. Med. Chem., Coll. Pharm., Boston, MA, 02115, USA
SOURCE: Analytical Chemistry (1984), 56(13), 2512-17
CODEN: ANCHAM; ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pentafluorobenzenesulfonyl chloride (PBSC) is a new reagent for electrophore labeling of small tyrosyl peptides, particularly onto their phenolic hydroxyl group, for anal. by gas chromatog. with electron capture
detection (GC-ECD). The products resist aqueous hydrolysis and have a response by GC-ECD close to that of lindane, a strong electrophore. Also examined are the peak asymmetry and response characteristics of these products as a function of the electrophore attachment site(s), N-Me vs. N-pivaloyl nonpolar derivatization, number of active hydrogens, and changes
in the GC-ECD equipment. Detection of 100 fg of the derivatized dipeptide
N-pivaloyl-O-[(pentafluorophenyl)sulfonyl]glycyltyrosine Et ester lowers the detection limit for peptide GC by 103.

IT 91860-44-5P 91860-45-6P 91860-46-7P
91860-47-8P 91860-50-3P 91860-51-4P
91860-52-5P
RL: PREP (Preparation)
(preparation and gas chromatog. with electron capture detection of)

RN 91860-44-5 CAPLUS
CN L-Tyrosine, N-acetyl-, ethyl ester, pentafluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

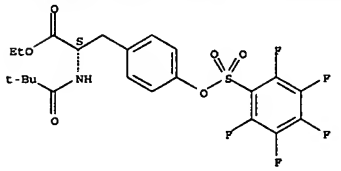
Absolute stereochemistry.



RN 91860-45-6 CAPLUS
CN L-Tyrosine, N-(2,2-dimethyl-1-oxopropyl)-, ethyl ester, pentafluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

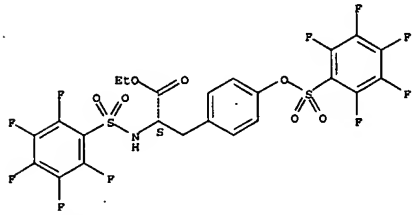
Absolute stereochemistry.

L4 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



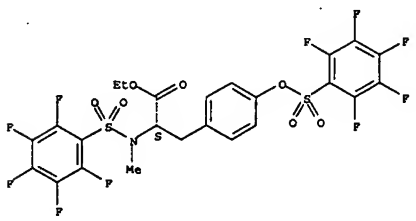
RN 91860-46-7 CAPLUS
CN L-Tyrosine, N-[(pentafluorophenyl)sulfonyl]-, ethyl ester, pentafluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 91860-47-8 CAPLUS
CN L-Tyrosine, N-methyl-N-[(pentafluorophenyl)sulfonyl]-, ethyl ester, pentafluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

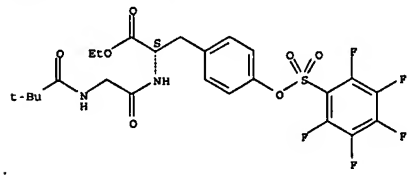
Absolute stereochemistry.



L4 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

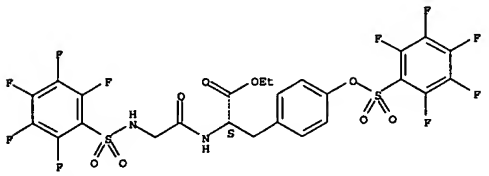
RN 91860-50-3 CAPLUS
CN L-Tyrosine, N-[N-(2,2-dimethyl-1-oxopropyl)glycyl]-, ethyl ester, pentafluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 91860-51-4 CAPLUS
CN L-Tyrosine, N-[N-[(pentafluorophenyl)sulfonyl]glycyl]-, ethyl ester, pentafluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

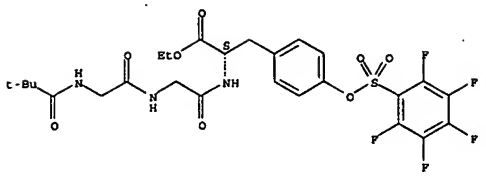
Absolute stereochemistry.



RN 91860-52-5 CAPLUS
CN L-Tyrosine, N-[N-[N-(2,2-dimethyl-1-oxopropyl)glycyl]glycyl]-, ethyl ester, pentafluorobenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1981:599739 CAPLUS
DOCUMENT NUMBER: 95:199739
TITLE: Lysine and tyrosine in the NADH inhibitory site of bovine liver glutamate dehydrogenase
AUTHOR(S): Saradambal, K. V.; Bednar, Rodney A.; Colman, Roberta F.
CORPORATE SOURCE: Dep. Chem., Univ. Delaware, Newark, DE, 19711, USA
SOURCE: Journal of Biological Chemistry (1981), 256(22), 11866-72
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

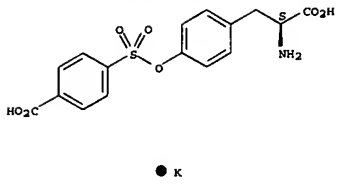
AB Native glutamate dehydrogenase is inhibited by high concns. of NADH by binding at a regulatory site distinct from the catalytic site. The enzyme reacts covalently with 5'-p-fluorosulfonylbenzoyladenosine (I) with complete loss of inhibition by NADH; a plot of initial velocity vs. NADH concentration for the modified enzyme contrasts markedly with that for the native enzyme in that it appears to obey normal Michaelis-Menten kinetics. The rate constant for loss of NADH inhibition, 0.0439 min-1 at 0.3 mM I, is not affected by GTP alone, but is decreased to 0.0096 min-1, by 3.1 mM NADH and essentially to 0 by 3.1 mM NADH plus 0.1 mM GTP. Upon reaction at a protein concentration of 2 mg/mL, only 0.53 mol of radioactive reagent are incorporated per peptide chain when the enzyme becomes unresponsive to NADH inhibition. The modified amino acids were purified by thin-layer electrophoresis with final separation being accomplished on an amino acid analyzer. Anal. pure samples of Nε-(4-carboxybenzenesulfonyl)lysine (II) and O-(4-carboxybenzenesulfonyl)tyrosine (III) were synthesized and characterized. These were the only unusual amino acids detected in samples of glutamate dehydrogenase and together could account for the total incorporation of radioactivity into the enzyme. As a function of time of incubation of enzyme with I, the product ratio of III to (II plus III) remains essentially constant at 0.47, with 0.25 mol of III and 0.28 mol of II being detected upon complete reaction. Apparently, both tyrosine and lysine are present in the NADH inhibitory site, and covalent modification of either residue on 3 of the 6 peptides of the catalytically active hexameric enzyme is sufficient to eliminate NADH inhibition.

IT 79864-53-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 79864-53-2 CAPLUS
CN L-Tyrosine, 4-carboxybenzenesulfonate (ester), monopotassium salt (9CI) (CA INDEX NAME)

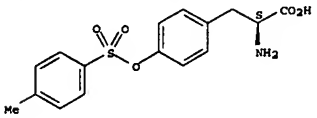
Absolute stereochemistry.

L4 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



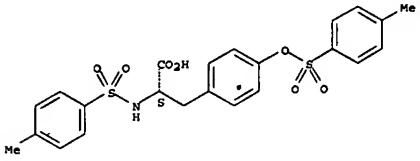
L4 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:400283 CAPLUS
DOCUMENT NUMBER: 89:283
TITLE: Arylsulfonate esters of fatty alcohols. II. Structural relation to hypocholesterolemic activity
AUTHOR(S): Quackenbush, Forrest W.; Grogan, W. McLean, Jr.; Midland, Sharon L.; Bell, Frank P.; MacNintch, John E.; Hutsell, Thomas C.; Cruzan, George; Klauda, Harry C.
CORPORATE SOURCE: Dep. Biochem., Purdue Univ., West Lafayette, IN, USA
SOURCE: Artery (Fulton, MI, United States) (1977), 3(6), 553-75
CODEN: ARTEDR; ISSN: 0098-6127
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ninety-three arylsulfonates RSO3R1 [R = Ph, substituted Ph, 2-naphthyl, cyclohexyl, cyclohexenyl, cyclohexadienyl, 3-pyridyl, 5-indanyl; R1 = alkyl, alkenyl, alkynyl, alkadienyl, 2,6-(MeO)2C6H3, cholesteryl] were prepared and tested for hypocholesterolemic activity in cholesterol fed rats. Oleyl p-decylbenzenesulfonate [56401-66-2] was the most effective in reducing cholesterol in plasma and liver. In long term expts., rabbits responded similarly to rats and showed possible regression of atheromatous lesions. Structure-activity relations were also discussed.
IT 13504-89-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and anticholesteremic activity of)
RN 13504-89-7 CAPLUS
CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:577453 CAPLUS
DOCUMENT NUMBER: 87:177453
TITLE: Antineoplastic agents. 2. Structure-activity studies on N-protected vinyl, 1,2-dibromoethyl, and cyanomethyl esters of several amino acids
AUTHOR(S): Loeffler, Larry J.; Sajadi, Ziaodin; Hall, Iris H.
CORPORATE SOURCE: Sch. Pharm., Univ. North Carolina, Chapel Hill, NC, USA
SOURCE: Journal of Medicinal Chemistry (1977), 20(12), 1584-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thirty title derivs. of tyrosine, tryptophan, glycine, leucine, proline, aspartic acid, glutamic acid, 4-aminobutyric acid, and 6-aminocaproic acid were prepared and tested, along with several analogs and reference compds., for in vivo antitumor activity. The most active compds., N-carbobenzoxyglycine 1,2-dibromoethyl ester (I) [64187-25-3] and N-carbobenzoxy-L-leucine 1,2-dibromoethyl ester [64187-28-6] were 100% and 99% effective resp., against Ehrlich ascites carcinoma, while only I was active against Walker 256 ascites carcinosarcoma, and none were active against P388 lymphocytic leukemia. Structure-activity relations are discussed.
IT 13504-90-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of)
RN 13504-90-0 CAPLUS
CN L-Tyrosine, N-[(4-methylphenyl)sulfonyl]-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

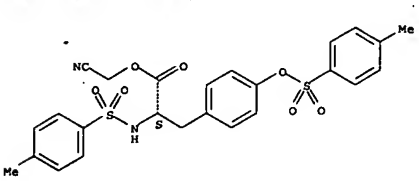
Absolute stereochemistry.



IT 64187-19-5P 64187-20-8P 64187-21-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and neoplasm inhibiting activity of)
RN 64187-19-5 CAPLUS

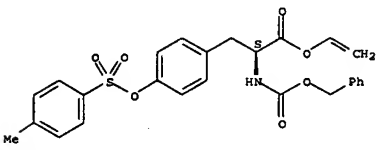
L4 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN L-Tyrosine, N-[(4-methylphenyl)sulfonyl]-, cyanomethyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



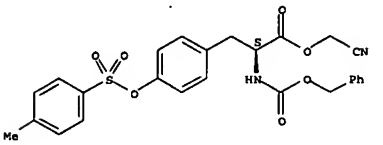
RN 64187-20-8 CAPLUS
CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-, ethenyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

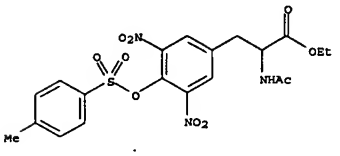


RN 64187-21-9 CAPLUS
CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-, cyanomethyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



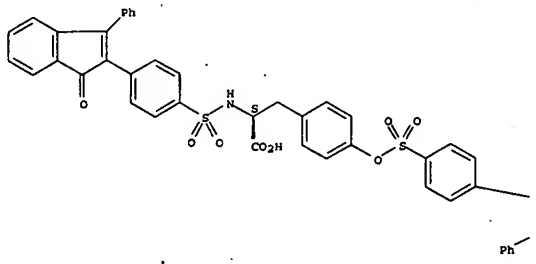
L4 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1974:141277 CAPLUS
DOCUMENT NUMBER: 80:141277
TITLE: Thyroid hormone analogs
AUTHOR(S): Ahmad, Parvez
CORPORATE SOURCE: Dep. Biochem., Univ. Dacca, Dacca, Bangladesh
SOURCE: Dacca University Studies (1971), 19(Pt. B), 65-72
CODEN: DUSTAG; ISSN: 0011-5223
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 2',3'-Diethyl-3,5-diiodo-DL-thyronine (I) [51554-02-0], 2',5'-diethyl-3,5-diiodo-DL-thyronine [51554-03-1], and butyl 3,5-diiodo-4-hydroxybenzoate [51-38-7] were prepared and the 1st 2 compds. were thyromimetic at a dose of 3 mg/kg in the rat. Butyl 3,5-diiodo-4-hydroxybenzoate was active as a thyroxine [51-48-9] antagonist showing 80% reversal of thyroxine at a molar ratio of 500 to 1.
The 2 diethyl analogs showed no antagonistic activity. Thus, substitution of ethyl groups at the 2',3', and 5' positions of thyroxine allowed for retention of thyromimetic activity.
IT 52211-54-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with diethyl phenols)
RN 52211-54-8 CAPLUS
CN Tyrosine, N-acetyl-3,5-dinitro-, ethyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)



L4 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1971:142329 CAPLUS
DOCUMENT NUMBER: 74:142329
TITLE: Preparation of sulfoindonyl derivatives of α-amino acids containing also another functional group
AUTHOR(S): Ivanov, Chavdar; Vladovska-Yukhnovska, Y.
CORPORATE SOURCE: Dep. Org. Chem., Inst. Chem. Technol., Sofia, Bulg.
SOURCE: Doklady Bolgarskoi Akademii Nauk (1971), 24(2), 207-10
CODEN: DBANAD; ISSN: 0366-8681
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Trifunctional amino acids are treated with 2-(p-chlorosulfonylphenyl)-3-phenylindone (I) in the presence of KOH or Na2CO3 to give II. Thus, serine reacts with I to give II (R = CH2OH). Similarly prepared are III, the Nε-sulfonyl lysine, the N,N'-disulfonyl lysine, and the N,O-disulfonyl tyrosine.
IT 32245-68-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 32245-68-4 CAPLUS
CN Tyrosine, N-[[p-(1-oxo-3-phenylinden-2-yl)phenyl]sulfonyl]-, p-(1-oxo-3-phenylinden-2-yl)benzenesulfonate (ester), L- (8CI) (CA INDEX NAME)

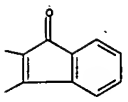
Absolute stereochemistry.

PAGE 1-A



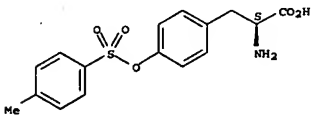
L4 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-B



L4 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:29263 CAPLUS
DOCUMENT NUMBER: 70:29263
TITLE: The syntheses of L-amino acids. IV. A synthesis of L-phenylalanine from L-tyrosine
AUTHOR(S): Kishi, Teruo; Kato, Yo; Tanaka, Masao
CORPORATE SOURCE: Kyowa Hakko Kogyo Co., Ltd., Tokyo, Japan
SOURCE: Nippon Nogei Kagaku Kaishi (1968), 42(4), 238-41
CODEN: NNKKAA; ISSN: 0002-1407
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB L-Phenylalanine (I) was prepared in the yield of about 55% by the catalytic reduction of O-tosyl-L-tyrosine (II) with Raney Ni catalyst in alkaline medium. No change of configuration occurred. In the reaction mixture some tyrosine can be detected. I was isolated from the reaction mixture by the treatment with a cation-exchange resin and the fractional crystallization The reduction of ditosyl-L-tyrosine gave N-tosyl-L-phenylalanine. An improved method for the preparation of II is also reported.
IT 13504-89-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 13504-89-7 CAPLUS
CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

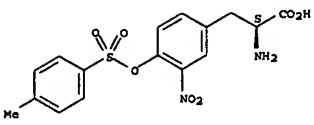
Absolute stereochemistry.



L4 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:497162 CAPLUS
DOCUMENT NUMBER: 69:97162
TITLE: Amino acids and peptides. I. Synthesis of fully protected nonapeptides of the oxytocin sequence with 3-nitro-L-tyrosine in position 2
AUTHOR(S): Kaurov, O. A.; Martynov, V. F.; Morozov, V. B.
CORPORATE SOURCE: Leningrad. Gos. Univ., Leningrad, USSR
SOURCE: Zhurnal Obshchei Khimii (1968), 38(4), 720-3
CODEN: ZOKHA4; ISSN: 0044-460X
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Treatment of 6.8 g. 3-nitro-L-tyrosine (I) in 60 cc. N NaOH with aqueous CuSO4 (2.4 g./16 cc.) and 5.7 g. p-MeC6H4SO2Cl in 12 cc. Et2O 3.5 hrs., followed by addition of 60 cc. concentrated HCl, gave 51% HCl salt (II) of O-tosyl-3-nitro-L-tyrosine, m. 197-8°, [α]1D7 -20.4° (c 0.3, HCONMe2). Passing dry HCl through a solution of 0.7 g. II in 4.55 cc. absolute EtOH 6 hrs. at 60° gave 95% HCl salt (III) of O-tosyl-3-nitro-L-tyrosine Et ester, m. 96-7.5°, [α]1D7 47° (c 0.21, HCONMe2). Reaction at 0° of the free base of III (prepared by addition of 0.17 cc. Et3N to 0.53 g. III) and 0.695 g. carbobenzoxy-S-benzyl-L-cysteine (IV) with 0.465 g. dicyclohexylcarbodiimide (V) in tetrahydrofuran gave 85% carbobenzoxy-S-benzyl-L-cysteinyl-O-tosyl-3-nitro-L-tyrosien Et ester (VI), m. 69-71°, [α]1D7 -36.7° (c 0.57, HCONMe2). Analogous synthesis of carbobenzoxy-S-benzyl-L-cysteinyl-3-nitro-L-tyrosine Et ester, m. 137-8°, [α]1D7 32° (c 1.37, HCONMe2), from 0.666 g. I Et ester and 1 g. IV, using V, yielded only 44% of the pure product, presumably because of the side reactions of the unprotected OH group in I. Treatment of 0.17 g. VI in 10 cc. absolute EtOH with 0.3 cc. N2H4 gave 69% VI hydrazide, m. 178-9°. A solution of 0.072 g. VI hydrazide in 2 cc. Me2SO was treated at -10° with 0.07 cc. 10% aqueous NaNO2 and 0.2 cc. concentrated HCl and then neutralized with excess solid NaOH. Addition of the HBr salt of L-isoleucyl-L-glutaminyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-prolyl-L-leucylglycinamide, followed by neutralization with NaOH, gave 40% carboxy-S-benzyl-L-cysteinyl-O-tosyl-3-nitro-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-S - benzyl-L-cysteinyl-L-prolyl-L-leucylglycinamide, m. 194-6° (decomposition).
IT 19653-81-7P 19653-82-8P 19748-52-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 19653-81-7 CAPLUS
CN Tyrosine, 3-nitro-, p-toluenesulfonate (ester), monohydrochloride, L- (8CI) (CA INDEX NAME)

Absolute stereochemistry.

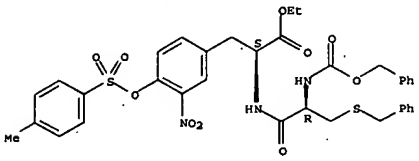
L4 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

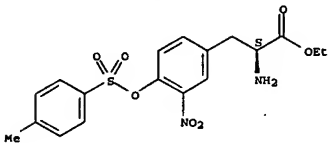
RN 19653-82-8 CAPLUS
CN Tyrosine, N-[3-(benzylthio)-N-carboxy-L-alanyl]-3-nitro-, N-benzyl ethyl ester, p-toluenesulfonate (ester), L- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 19748-52-8 CAPLUS
CN Tyrosine, 3-nitro-, ethyl ester, p-toluenesulfonate (ester), monohydrochloride, L- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L4 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L4 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1968:22233 CAPLUS
DOCUMENT NUMBER: 68:22233
TITLE: Insulin peptides. I. Protected peptides with sequences derived from the A-chain of ovine insulin
AUTHOR(S): Stewart, Frederick H. C.
CORPORATE SOURCE: Div. Protein Chem., C.S.I.R.O., Parkville, Australia
SOURCE: Australian Journal of Chemistry (1967), 20(9), 1991-2002
CODEN: AJCHAS; ISSN: 0004-9425
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Syntheses are described of two pentapeptide derivs. with the A5-9 and A17-21 sequences, resp., of ovine insulin, and of a protected tetrapeptide with a modified A1-4 sequence. Preparation of the three compds. involved the use of the 2,4,6-trimethylbenzyl carboxyl-protecting group in conjunction with the o-nitrophenylsulfenyl and benzyloxycarbonyl amino-protecting groups. 39 references.

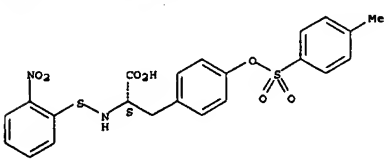
IT 15396-66-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 15396-66-4 CAPLUS
CN Tyrosine, N-[(o-nitrophenyl)thio]-, p-toluenesulfonate (ester), compd. with dicyclohexylamine (1:1), L- (8CI) (CA INDEX NAME)

CM 1

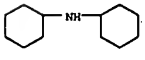
CRN 47732-68-3
CMF C22 H20 N2 O7 S2

Absolute stereochemistry.



CM 2

CRN 101-83-7
CMF C12 H23 N



L4 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

SAEED

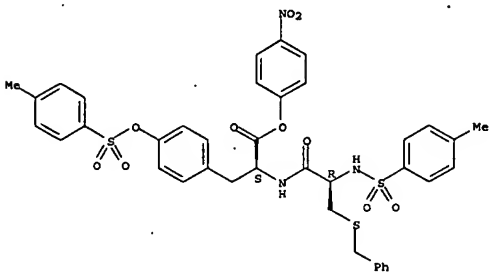
L4 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:444069 CAPLUS
DOCUMENT NUMBER: 67:44069
TITLE: Amino acids and peptides. LXXII. Synthesis of 2-phenylalanine-[U-14C] 8-lysine vasopressin
AUTHOR(S): Thomas, Patrick Jonathan; Havranek, M.; Rudinger, Josef
CORPORATE SOURCE: Ceskoslov. Akad. Ved, Prague, Czech.
SOURCE: Collection of Czechoslovak Chemical Communications (1967), 32(5), 1767-75
CODEN: CCCCAK; ISSN: 0010-0765
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CA 66: 86017h. In this abstract, Z = benzyloxycarbonyl, BZL = PhCH2, TOS = tosyl, NPS = o-nitrophenylsulfenyl, Np = p-C6H4NO2; all amino acids are of the L configuration. Z-Phe (19.0 mg.), obtained in 88.5% yield from the labeled amino acid, was shaken in 0.29 ml. MeCN and 24.62 mg. N-methylpiperidine with 16.8 mg. 2-ethyl-5-phenylisoxazolium 3'-sulfonate until dissolved, 61.9 mg. Gln-Asn-Cys(BZL)-Pro-Lys(TOS)-Gly-NH2 in 0.55 ml. HCONMe2 added and the mixture kept 24 hrs. to give 64.7 mg. Z-Phe-Gln-Asn-Cys(BZL)-Pro-Lys(TOS)-Gly-NH2 (I), m. 182-8°. Treating I with 0.7 ml. 35% HBr solution in AcOH gave 71% Phe-Gln-Asn-Cys(BZL)-Pro-Lys(TOS)-Gly-NH2 (II), m. 130-5°. II (41.1 mg.) was coupled as usual with TOS-Cys(BZL)-Tyr-N3 (from 215.5 mg. hydrazile) to give 39 mg. TOS-Cys(BZL)-Tyr-Phe-Gln-Asn-Cys(BZL)-Pro-Lys(TOS)-Gly-NH2, m. 187-95°, which was treated with Na in liquid NH3 to give the title compound (III) in 8.5% overall yield (specific radioactivity 5.8 c./mg., radioactivity: pressor activity 2.60 mμc./I.U.). By an alternative route, NPS-Tyr(BZL), m. 136-9°, gave with p-O2NC6H4OH and dicyclohexylcarbodiimide in AcOEt 76% NPS-Tyr(BZL)-ONp, m. 148-54°, which was converted with 7M HCl-Et2O to 90% Tyr(TOS)-ONp.HCl, m. 155-65°, and this, in turn, shaken with TOS-Cys(BZL)-Cl to yield 79% TOS-Cys(BZL)-Tyr(BZL)-ONp (IV), m. 166-7°. IV (45 mg.) was coupled with 31.3 mg. II to give 64% TOS-Cys(BZL)-Tyr(BZL)-Phe-Gln-Asn-Cys(BZL)-Pro-Lys(TOS)-Gly-NH2, m. 190-200°, [α]25D -26.2° (c 0.5, HCONMe2), yielding as above III in 13.7% overall yield. As a variation of the 2nd method, NPS-Tyr(TOS), m. 144-8°, was converted to 58% NPS-Tyr(TOS)-ONp, m. 119-21°, which treated with 6.85M HCl-Et2O and the HCl salt of Tyr(TOS)-ONp, m. 175-80°, acylated as above to give 56% TOS-Cys(BZL)-Tyr(TOS)-ONp, m. 128-31°, or coupled with II to yield 84% TOS-Cys(BZL)-Tyr(TOS)-Phe-Gln-Asn-Cys(BZL)-Pro-Lys(TOS)-Gly-NH2, m. 180-92°, [α]D -29.3° (c 0.5, HCONMe2).
IT 15396-66-4P 15396-85-7P 15396-86-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 15396-66-4 CAPLUS
CN Tyrosine, N-[(o-nitrophenyl)thio]-, p-toluenesulfonate (ester), compd. with dicyclohexylamine (1:1), L- (8CI) (CA INDEX NAME)

CM 1

CRN 47732-68-3
CMF C22 H20 N2 O7 S2

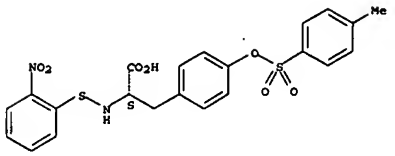
L4 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN Tyrosine, N-[3-(benzylthio)-N-(p-tolylsulfonyl)-L-alanyl]-, p-nitrophenyl ester, p-toluenesulfonate (ester), L- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



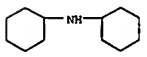
L4 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



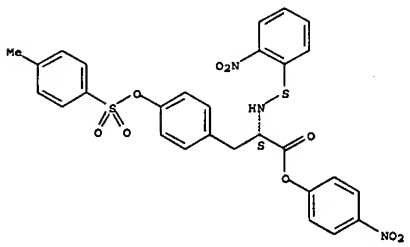
CM 2

CRN 101-83-7
CMF C12 H23 N



RN 15396-85-7 CAPLUS
CN Tyrosine, N-[(o-nitrophenyl)thio]-, p-nitrophenyl ester, p-toluenesulfonate (ester), L- (8CI) (CA INDEX NAME)

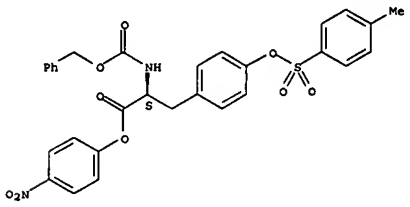
Absolute stereochemistry.



RN 15396-86-8 CAPLUS

L4 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:46576 CAPLUS
DOCUMENT NUMBER: 66:46576
TITLE: A synthesis of two protected nonapeptide amides with the amino acid sequence of oxytocin
AUTHOR(S): Stewart, Frederick H. C.
CORPORATE SOURCE: Div. Protein Chem., C.S.I.R.O., Parkville, Australia
SOURCE: Australian Journal of Chemistry (1966), 19(12), 2361-72
CODEN: AJCHAS; ISSN: 0004-9425
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two protected nonapeptide amides with the amino acid sequence of oxytocin were synthesized by a route involving the use of benzyloxycarbonyl peptide p-nitrophenyl esters as coupling components. One of the products is a compound which was described previously, and converted into oxytocin, by various authors. The present approach is discussed in relation to the earlier syntheses. 43 references.
IT 14485-86-0P 14485-87-1P 14485-89-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 14485-86-0 CAPLUS
CN Tyrosine, N-carboxy-, N-benzyl p-nitrophenyl ester, p-toluenesulfonate (ester), L- (8CI) (CA INDEX NAME)

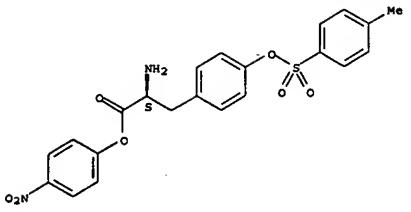
Absolute stereochemistry.



RN 14485-87-1 CAPLUS
CN Tyrosine, L-, p-nitrophenyl ester, p-toluenesulfonate (ester), monohydrobromide (8CI) (CA INDEX NAME)

Absolute stereochemistry.

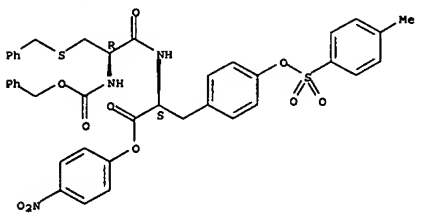
L4 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



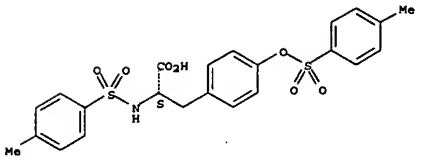
● HBr

RN 14485-89-3 CAPLUS
CN Tyrosine, N-[3-(benzylthio)-N-carboxy-L-alanyl]-, N-benzyl p-nitrophenyl ester, p-toluenesulfonate (ester), L- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

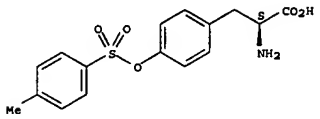


L4 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:11178 CAPLUS
DOCUMENT NUMBER: 66:11178
TITLE: L-Phenylalanine
PATENT ASSIGNEE(S): Kyowa Fermentation Industry Co., Ltd.
SOURCE: Fr., 5 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1438616		19660513	FR 1965-13901	19650420
DE 1493900			DE	
GB 1078557			GB	
JP 42002695		19670000	JP	
US 3410896		19681112	US 1965-449643	19650420
PRIORITY APPLN. INFO.:			JP	19640421

AB The title compound is prepared by reductive removal of the OH group of L-tyrosine while maintaining optical activity. O-Tosyl-L-tyrosine (34 g.) in 500 ml. 2% NaOH and 500 ml. EtOH treated 1 hr. with H in the presence of 40 g. Raney Ni at room temperature until 2.5 l. H is absorbed, the reaction mixture filtered and acidified to pH 2, and the product treated with an acid exchange resin yielded 15 g. L-phenylalanine, m. 282°, [α] 20 D -35.0° (c = 2, H2O). Similarly prepared are N-tosyl-L-alanine, m. 163°, [α] 20 D -21° (c = 2, MeOH) and acetyl-L-phenylalanine, 170°.
IT 13504-89-7 13504-90-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(in manufacture of phenyl-L-alanine)
RN 13504-89-7 CAPLUS
CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 13504-90-0 CAPLUS
CN L-Tyrosine, N-[(4-methylphenyl)sulfonyl]-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1964:425736 CAPLUS
DOCUMENT NUMBER: 61:25736
ORIGINAL REFERENCE NO.: 61:4475c-h,4476a-h,4477a-b
TITLE: Peptide syntheses. XXIX. N-Substituted derivatives of asparagine and aspartic acid β-tert-butyl ester
AUTHOR(S): Schroeder, Eberhard; Klieger, Erich
SOURCE: Ann. (1964), 673, 208-20
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 61:25736
AB (The abbreviations used are described in the preceding parts; all amino acids have the L-configuration). RO2CCH(NHR1)CH2CO2R2 (I) (R = PhCH2, R1 = R2 = H) (II) (28.2 g.) in 1.92 l. tert-BuOAc and 12.8 cc. HClO4 stirred 1 h. to complete solution, and the solution kept 4 days at room temperature and worked up gave 28 g. I (R = PhCH2, R1 = H, R2 = tert-Bu) HCl salt (III.HCl), m. 109-10° (EtOAc-petr. ether), [α]25D -8.7° (c 0.7, MeOH). Cbo-Aspartic anhydride (172 g.) in 240 cc. absolute THF treated with 116 g. p-O2NC6H4CH2OH (IV) and 200 cc. dicyclohexylamine (V) in 450 cc. absolute Et2O, 160 cc. Et2O added, and the mixture kept overnight at room temperature gave 273 g. crude I (R = p-O2NC6H4CH2, R1 = Cbo, R2 = H) (VI) DCHA salt (VII), m. 155-6°, [α] 25D - 11.1° (c 1, 95% AcOH), m. 153-4° (EtOH), [α]25D - 11.7° (c 1, 95% AcOH). Crude VII (4.7 g.) kept 3 days at room temperature with concentrated aqueous NH3 and worked up gave 1.41 g. Cbo-isoasparagine, m. 164° (HCO2H-H2O), [α]25D -25.5° (c 1, DMF). VI (4.0 g.) kept 30 min. at room temperature with 10 cc. 36% AcOH-HBr and worked up gave 1.8 g. I (R = p-O2NC6H4CH2, R1 = R2 = H) (VIII), m. 172-3° (H2O), [α]25D- 15.1° (c 1, N HCl). VI (20 g.) in 150 cc. CH2Cl2 shaken 4 days at room temperature with 0.5 cc. concentrated H2SO4 and 25 cc. Me2C:CH2 in a pressure flask and the solution worked up gave 18 g. I (R = PhCH2, R1 = Cbo, R2 = tert-Bu) (IX), m. 93-4° (EtOAc-petr. ether), [α]25D -16.6° (c 1, MeOH). IX (3.2 g.) stirred 1 h. at room temperature in 25 cc. Me2CO containing 7.7 cc. N NaOH and the solution worked up gave 2.3 g. I (R = H, R1 = Cbo, R2 = tert-Bu), oil; DCHA salt m. 123-4° (Me2CO-Et2O), [α]25D 7.7° (c 1, 90% AcOH). IX (2.3 g.) in 50 cc. MeOH hydrogenated over Pd-black and the filtered solution evaporated gave 0.72 g. I (R = R1 = H, R2 = tert-Bu) (X), m. 197° (decomposition) (MeOH-Et2O), [α]25D 7.5° (c 1, 90% AcOH) and 8.3° (c 1, H2O). I(R = H, R1 = Cbo, R2 = Me)(2.8 g.)in 10 cc. THF combined with 1.56 g. tert-BuO2CNHNH2 in THF, 2.47 g. dicyclohexylcarbodiimide (XI) added, and the solution kept several hrs. at 0° overnight at room temperature, and worked up gave 1.84 g. I (R = H2NNH, R1 = Cbo, R2 = Me), m. 129-30° (MeOH), [α]25D-17.5°(c 1, DMF). I(R = R1 = R2 = H) (86 g.) in 600 cc. H2O shaken 4 days at room temperature with 76.8 g. MgO and 103.4 g. tert-BuOCON3 (XII) in 400 cc. dioxane and worked up gave 51.5 g. I(R = R2 = H, R1 = BOC)(XIII), m. 118-19°, [α]25D -6.2° (c 1, MeOH); bis-DCHA salt m. 176-7° (EtOH-Et2O-petr. ether), [α]25D 10.9° (c 1, MeOH). XIII (23.3 g.) in 50 cc. absolute THF kept 6 h. at 0° with 22.7 g. XI in 40 cc. absolute THF and the filtered solution evaporated gave 19.7 g. BOC-aspartic anhydride (XIV), m. 133-4°

L4 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(dry Me2CO-petr. ether), [α]25D 38.9° (c 1, AcOH). XIII (1.16 g.) in 8 cc. abs. THF kept 4 days at room temp. with 1 cc. EtCOC.tplbond.CH (XV) in a closed vessel and the soln. evapd. gave 0.6 g. XIV, m. 134-5° (Me2CO-Et2O-petr. ether), [α]25D -38.2° (c 1, AcOH). XIII (2.15 g.) in 8 cc. abs. THF stirred 30 min. at room temp. with 1.65 g. IV, 2.2 cc. V added, and the soln. dild. to 200 cc. with abs. Et2O, stirred several hrs., and kept overnight pptd. 4.4 g. I (R = p-O2NC6H4CH2, R1 = BOC, R2 = H) (XVI) DCHA salt, m. 166-7° (EtOH), [α]25D -11.7° (c 1, DMF), converted into 54% XVI, m. 135-6° (EtOAc-petr. ether), [α]25D -8.5° (c 0.48, MeOH), which gave VIII with CF3CO2H (30 min. at room temp.). Similarly was prepd. 53% I (R = Et, R1 = BOC, R2 = H) DCHA salt, m. 136-7° (H2O), [α]25D -8.1° (c 1, DMF). Isoasparagine (1.32 g.) in 15 cc. H2O shaken 5 days at room temp with 0.8 g. MgO and 2 g. XII in 15 cc. dioxane and the mixt. worked up gave 1.3 g. BOC-isoasparagine, m. 153-5° (EtOH-Et3O-petr. ether), [α] 25D -31.3° (c 1, DMF). RO2CCH(NHR1)CH2CONH2 (XVII) (R = R1 = H) (XVIII) (9 g.), 4.8 g. MgO, and 12 g. XII in 180 cc. 1: 1 H2O-dioxane shaken 4 days at room temp. and worked up gave 10 g. XVII (R = H, R1 = BOC) (XIX), m. 181-2° (EtOH-H2O), [α]25D - 7.8° (c 1, DMF). XIX (4.6 g.) in 50 cc. THF and 15 cc. DMF kept 6 h. at 0° with 3.1 g. p-O2NC6H4OH (XX) and 4.5 g. XI and the filtered soln. worked up gave 3.65 g. XVII (R = p-O2NC6H4, R1 = BOC), m. 157-8° (EtOH), [α]25D -45.30° (c 1, DMF). III (from 12.7 g. III.HCl in THF with 6.4 cc. Et3N) in 12 cc. C5H5N stirred 2 days at room temp. with 7.5 g. XII and worked up gave 12 g. I (R = PhCH2, R1 = BOC, R2 = tert-Bu) (XXI), m. 54-5° (aq. EtOH), [α]25D -21.4° (c 1, MeOH). XXI (19.0 g.) hydrogenated in 500 cc. MeOH over Pd-black gave I (R = H, R1 = BOC, R2 = tert-Bu) (XXII), m. 63-4° (petr. ether), [α]25D -21.7° (c 1, DMF); DCHA salt (XXIII) m. 144-5° (H2O-EtOH), [α]25D 16.6° (c 1, MeOH). XXI (1.9 g.) stirred 2 h. at room temp. in 20 cc. Me2CO contg. 5 cc. N NaOH and worked up gave 1.4 g. XXII, oil; XXIII m. 139-40°, [α] 25D 16.2° (c 1, MeOH). I (R = R2 = H, R1 = MCbo) (XXIV) (8.9 g.) in 30 cc. abs. THF treated with 6.8 g. XI in 25 cc. abs. THF, and the soln. kept 5 h. at 0° and worked up gave 5.8 g. MCbo-aspartic anhydride (XXV), m. 136-7° (Me2CO-petr. ether), [α]25D -38.8° (c 1, AcOH). XXIV treated with XV like XIV gave 50% XXV, m. 137-8° (Me2CO-Et2O-petr. ether), [α]25D -36.8° (c 1, AcOH). XXV (1.95 g.) in a little abs. THF treated with 2 cc. PhCH2OH and 1.6 cc. V gave 1.9 g. I (R = PhCH2, R1 = MCbo, R2 = H), m. 150-1° (EtOH); DCHA salt (XXVI) m. 105-6° (EtOAc-petr. ether), [α]25D -15.6° (c 1, MeOH). II (4.46 g.) and 1.6 g. MgO in 40 cc. H2O shaken 4 days at room temp. with 4.6 g. p-MeOC6H4CH2OCON3 (XXVII) and the mixt. worked up gave 2.2 g. XXVI, m. 105-6° (EtOH-Et2O-petr. ether), [α]25D -15.4° (c 1, MeOH). From 2.44 g. XXV, 1.4 g. IV, and 2 cc. V was prepd. 3.3 g. I (R = p-O2NC6H4CH2, R1 = Mcbo, R2 = H) (XXVIII) DCHA salt, m. 160-1° (EtOH), [α]25D -12.4° (c 1, AcOH), converted into 81% XXVIII, m. 118-19° (EtOAc-petr. ether), [α]25D -16.0° (c 1, MeOH), which gave VIII with CF3CO2H-PhOMe (20 min. at room temp.). XXV

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(1.95 g.) in 3 cc. abs. THF treated with 5 cc. EtOH and 1.6 g. V gave 1.8 g. I (R = Et, R1 = MCbo, R2 = H) DCHA salt, m. 150-1° (EtOH), [α]25D -7.9° (c 1, DMF), which gave I (R = Et, R1 = R2 = H) after treatment with CF3CO2H-PhOMe (20 min. at room temp.). XVIII.H2O (6.0 g.) and 3.2 g. MgO in 80 cc. H2O shaken 4 days at room temp. with 11.2 g. XXVII in 80 cc. dioxane in a closed vessel gave 6.7 g. XVII (R = H, R1 = MCbo) (XXIX), m. 158-9° (EtOH-Et2O), [α]25D -5.3° (c 1, MeOH) and -4.5° (c 1, DMF). From 1.32 g. isoasparagine and 0.8 g. MgO in 20 cc. H2O and XXVII in 20 cc. dioxane was similarly prepd. 2.3 g. MCbo-isoasparagine, m. 144-6° (MeOH-Et2O-petr. ether), [α]25D -25.4° (c 1, DMF). XXIX (0.89 g.) in 10 cc. THF and 2 cc. DMF kept 6 h. at 0° with 0.56 g. XX and 0.82 g. XI in THF and the mixt. worked up gave 0.6 g. XVII (R = p-O2NC6H4, R1 = MCbo), m. 161-2° (EtOH), [α]25D -30.9° (c 1, DMF). III (from 22.1 g. III.HCl in THF with 10 cc. Et3N) in 21 cc. C5H5N stirred 3 days at room temp. with 19.6 g. XXVII and the soln. worked up gave 18.5 g. I (R = PhCH2, R1 = MCbo, R2 = tert-Bu) (XXX), m. 70.5-1.0° (Et2O-petr. ether), [α]25D -17.3° (c 1, MeOH). XXX (2.2 g.) stirred 2 h. at room temp. in 20 cc. Me2CO contg. 5 cc. N NaOH and worked up gave 1.8 g. crude I (R = H, R1 = MCbo, R2 = tert-Bu), oil, converted into 75% DCHA salt (XXXI), m. 127-8° (EtOH-Et2O-petr. ether), [α]25D 9.1° (c 1, MeOH). From 1.9 g. X and 0.8 g. MgO in 20 cc. H2O and 2.3 g. XXVII in 20 cc. dioxane was prepd. 2.8 g. XXXI, m. 129.5-30.0° (EtOH-Et2O-petr. ether), [α] 25D 8.9° (c 1, MeOH). II (4.46 g.) and 5.8 g. Na2CO3.10H2O in 60 cc. H2O stirred 45 min. at room temp. with 4.6 g. o-C6H4(CO)2NCO2Et (XXXII), the soln. filtered, acidified with concd. HCl, and extd. with EtOAc, and the ext. dried; dild. with Et2O, and treated with 4.4 cc. V gave 7.6 g. I (R = PhCH2, R1 = phthalyl, R2 = H) (XXXIII) DCHA salt, m. 152-3° (EtOAc), [α]25D -26.2° (c 1, MeOH), which (4.3 g.) stirred 1 h. in 60 cc. MeOH and 30 cc. H2O with Dowex-50 (H form) and the mixt. worked up gave 1.9 g. XXXIII, m. 111-12° (EtOAc-petr. ether), [α]25D -45.7° (c 1, MeOH). VIII (1.08 g.) and 1.2 g. Na2CO3.10H2O in 20 cc. H2O treated similarly with 0.92 g. XXXII gave 1.0 g. I (R = p-O2NC6H4CH2, R1 = phthalyl, R2 = H), m. 148-9° (EtOAc-petr. ether), [α] 25D -62.0° (c 1, MeOH); DCHA salt m. 152-3° (EtOH-Et2O), [α]25D -38.8° (c 1, MeOH). XVIII.H2O (30.0 g.) and 57.5 g. Na2CO3.10H2O in 500 cc. H2O stirred 45 min. at room temp. with 50 g. XXXII and the soln. acidified gave 36 g. XVII (R = H, R1 = phthalyl) (XXXIV), m. 183-4° (H2O-EtOH), [α]25D -78.8° (c 1, EtOH). From 2.62 g. XXXIV, 1.54 g. XX, and 2.3 g. XI was prepd. as above 2.0 g. XVII (R = p-O2NC6H4, R1 = phthalyl), m. 150-1° (EtOAc-petr. ether, EtOH), [α]25D -117.5° (c 1, DMF). III.HCl (28.5 g.) in 130 cc. H2O stirred 1.5 h. at room temp. with 26.4 g. Na2CO3.10H2O and 25 g. XXXII and worked up gave 39.2 g. I (R = PhCH2, R1 = phthalyl, R2 = tert-Bu) (XXXV), m. 74-5° (Et2O-petr. ether), [α]25D -34.0° (c 1, MeOH). XXXV (39.0 g.) hydrogenated in 900 cc. MeOH over Pd-black gave 21.4 g. I (R = H, R1 = phthalyl, R2 = tert-Bu) (XXXVI), m. 112-13° (Et2O-petr. ether), [α]25D -50.8° (c 1,

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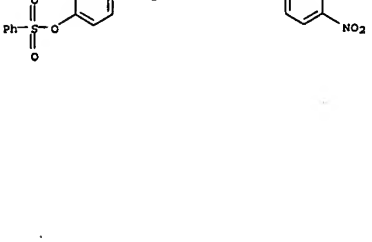
MeOH); DCHA salt m. 197-8° (EtOAc), [α]25D -22.7° (c 1, MeOH). XXXVI (9.6 g.), 5.1 g. XX, and 6.8 g. XI in THF kept 7 h. at 0° and the mixt. worked up gave 8.9 g. I (R = p-O2NC6H4, R1 = phthalyl, R2 = tert-Bu), m. 118-19° (EtOAc-petr. ether), [α]25D -86.4° (c 1, MeOH). I (R = R1 = R2 = H) (6.7 g.), 19.9 g. IV, and 10.3 g. PhSO3H in 1250 cc. CCl4 boiled 3 days with continuous removal of the water formed gave 17.7 g. I (R = R2 = p-O2NC6H4CH2, R1 = H) benzenesulfonate, m. 162-3° (MeOH with C), [α]25D -8.4° (c 1, C5H5N). The following benzenesulfonates of amino acid p-nitrobenzyl esters were prepd. similarly [amino acid, % yield, m.p., [α]25D (c 1, C5H5N) given]: glutamic acid (bis(p-nitrobenzyl)ester], 71, 152-3° (EtOH), 15.4°; glycine, 61, 191-2° (EtOH), -; leucine, 71, 213-15° (EtOH), 16.7°; serine, 60, 157-8° (EtOH), -14.4°; tyrosine, 60, 218-19° (95% MeOH), 15.2°; valine, 78, 155° (MeOH-Et2O), 15.1°; S-benzylcysteine, 60, 170-1° (90% EtOH), -20.5° (c 1, DMF).

IT 95292-22-1, Tyrosine, p-nitrobenzyl ester, benzenesulfonate (salt)
(preparation of)

RN 95292-22-1 CAPLUS

CN Tyrosine, p-nitrobenzyl ester, benzenesulfonate (7CI) (CA INDEX NAME)



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ACCESSION NUMBER: 1964:10005 CAPLUS
DOCUMENT NUMBER: 60:10005
ORIGINAL REFERENCE NO.: 60:1836h,1837a-h,1838a
TITLE: Usefulness of the phthalimidomethyi group for the reversible protection of carboxyl functions
AUTHOR(S): Nefkens, G. H. L.; Tesser, G. I.; Nivard, R. J. F.
CORPORATE SOURCE: R. C. Univ., Nijmegen, Neth.
SOURCE: Recueil des Travaux Chimiques des Pays-Bas (1963), 82(9-10), 941-53
CODEN: RTCPA3; ISSN: 0165-0513
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 60:10005

AB cf. CA 57, 47515. The usefulness of phthalimidomethyl esters in peptide synthesis was investigated. BzCl (2.32 mL.) added over 10 min. to a solution of 3.6 g. N-hydroxymethylphthalimide in 15 mL. dry pyridine at 0°, and the solution held 0.5 h. at 0° and 3 h. at room temperature gave 81% phthalimidomethyl benzoate (I), m. 127° (iso-PrOH). The stability of the ester bond in I (0.02 mol in 20-50 mL. of the appropriate solvent) was tested under a variety of reaction conditions used for removal of protecting groups from amino acids (reagent, reaction time, temperature, and product given): HCl in dioxane, 16 h., 20°, 82% BzOH (II); HCl in EtOAc, 18 h., 20°, 83% II; HBr in HOAc, 15 min., 20°, 80% II; excess Et2NH in alc., 3 h., 20°, 82% II; excess NH2NH2.H2O in alc., 3 h., 20°, 90% II; NaOH (2 mol) in aqueous alc., 45 min., 20°, 77% II; Na in liquid NH3, 30 min., -33°, undefined reaction products; pyridine-HCl in CHCl3, 24 h., 61°, 87% I recovered; pyridine-HBr in CHCl3, 24 h., 61°, 85% I recovered; dry p-toluenesulfonic acid in ethylene chloride, 5 h., 83°, 87% I recovered; dry LiBr in pyridine, 7 h., 116°, 76% I recovered; hydrogenation on Pd-C, 48 h., 17°, 90% I recovered. Phthalimidomethyl esters of N-substituted acids or peptides were synthesized by addition of 1 mol N-chloromethylphthalimide to 1 mol of the acid component dissolved in dry EtOAc containing 1 mol Et2NH, and holding the mixture overnight at 37-40°; with DMF (DMP) or DMSO as solvent and dicyclohexylamine as base, the reaction time at 60° could be reduced to a few min.; racemization did not occur in the reaction. Phthalimidomethyl esters of the c following amino acid and peptide derivs. were prepared [derivative (Z = N-benzyloxycarbonyl), m.p., % yield, and [α]23-5°D (c 2, unless indicated otherwise, DMF) given]: Z-glycine, 95-6°, 80, -; Z-DL-alanine, 124, 82, -; Z-L-leucine, 70-2°, 92, -14.4°; Z-L-proline, oil, 90, -; Z-L-phenylalanine, 131-3°, 85, -23.5° (c 1); β-benzyl Z-L-aspartate, 90-2°, 87, -10.0°; di-Z-L-tyrosine, 124°, 78%, -27.2°; Z-L-glutamic acid (diester), 147.5°, 70, -11.6° (c 2.5), Z-L-Leu-L-Leu, 90-1°, 79, -15.6°; Z-Gly-L-Phe, 140-2°, 81, 5.7°; phthaloyl-Gly-Gly, 214°, 85, -; γ-benzyl tosyl-L-glutamate, 176-8°, 74, -14.8°; α-benzyl tosyl-L-glutamate, 116-17°, 70, -5.5° (c 3); and Z-Gly-L-Leu, oil, 85, -. The phthalimidomethyl esters of the N-benzyloxycarbonylamino acid or peptide were dissolved in MeOH containing an equimolar amount of p-toluenesulfonic acid, and H was bubbled through the solution in the presence of Pd-C until no more

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CO2 evolved; the following p-toluenesulfonates of amino acid phthalimidomethyl esters were prepd. in this way [amino acid or peptide, m.p., % yield, and [α]25D (c 2 unless indicated otherwise, DMF) given]: glycine, 180-2°, 86, -; DL-alanine, 168-70°, 91, -; L-leucine, 207-8°, 68, 7.2° (c 1.5); L-proline, 165-7°, 72, -12.2°; L-phenylalanine, 214-15°, 93, -2.0°, L-aspartic acid (α-ester), 171-4°, 60, -0.2°; L-tyrosine, 198-200°, 77, -18.7°; Gly-L-Leu, 212-14°, 81, -17.3°. With β-benzyl α-phthalimidomethyl N-benzyloxycarbouyl-L-aspartate, the benzyl ester bond was also hydrolyzed. Usefulness of phthalimidomethyl esters of amino acids in the synthesis of peptidea was tested with a no. of the compds. just liated; in all cases N-benzyloxycarbonylglycine was used as carboxyl component; in general, the yields and purity of the products were good. The following new compds. were prepd. in this way: Z-Gly-Gly phthalimidomethyl ester, m. 118-19°, 91% yield; and Z-Gly-L-Phe phthalimidomethyl ester, m. 134-7°, 71% yield, [α]24D -5.5° (c 1, DMF). A slight exceas of p-toluenesulfonyl chloride was added to an alk. soln. of γ-benzyl L-glutamate, and the oily product was converted, by addn. of dicyclohexylamine to an alc. soln., to 43% dicyclohexylammonium γ-benzyl N-tosyl-L-glutamate, m. 185-90° (DMF), [α]22D 35.5° (c 1, CHCl3). α-Benzyl γ-phthalimidomethyl N-tosyl-L-glutamate (1.5 g.) hydrogenated 8 h. in EtOAc with Pd-C gave 99% γ-phthalimidomethyl N-tosyl-L-glutamate, m. 110-12°, [α]24D -0.7° (c 2, DMF); dicyclohexylammonium sslt m. 194-5°, [α]23D 38° (c 1, CHCl3). Dicyclohexylammonium α-phthalimidomethyl N-tosyl-L-glutamate (0.005M) dissolved in 10 mL. warm dry DMF, 900 mg. p-nitrobenzyl chloride added and the mixt. held several min. at 60° gave 2 g. γ-p-nitrobenzyl α-phthalimidomethyl N-tosyl-L-glutamate (III), m. 136-7° (EtOH), [α]23D -6.0° (c 2, DMF). N-Tosyl-L-glutamic acid (30.1 g.) dissolved in DMF, the mixt. heated with 36.2 g. dicyclohexylamine until soln. was complete, 35 g. p-nitrobenzyl chloride in DMF added, and the mixt. kept warm for several min. gave 60% α-γ-di-p-nitrobenzyl N-tosyl-L-glutamate (IV), m. 118° (EtOAc), [α]22D -9.0° (c 2, DMF). IV (0.01 mol) in 30 mL. dioxsne treated with 11 mL. N NaOH over 1 h., the soln. shaken 2 h., and the oily product in EtOH soln. converted to the salt by addn. of 1.81 g. dicyclohexylamine gave 3 g. dicyclohexylammonium γ-p-nitrobenzyl N-tosyl-L-glutamate (V), m. 189.5-91°, [α]22D 89.6° (c 1, CHCl3); V was also obtained in 78% yield from III with HBr in HOAc. Dicyelohexylammonium γ-tert-Bu N-benzyloxycarbonyl-L-glutamate (2.08 g.) dissolved in 15 mL. dry warm DMF, 0.79 g. N-chloromethylphthalimide added, and the mixt. held 1 h. at room temp. gave 85% γ-tert-Bu α-phthalimidomethyl N-benzyloxycarbonyl-L-glutamate (VI), m. 72° (iso-BuOH-petr. ether), [α]20D -13.7° (c 2, DMF). Refluxing a soln. of VI in C6H6 0.5 h. with p-toluenesulfonic acid monohydrate and conversion to the salt by addn. of dicyclohexylamine gave dicyclohexylammonium α-phthalimidomethyl N-benzyloxycarbonyl-L-glutamate, m. 150-3° (iso-PrOH). The phthalimidomethyl group was removed from VI in 1:1 MeOH-Et2N; the product on addn. of dicyclohexylamine gave 80% dicyclohexylammonium γ-tert-Bu N-benzyloxycarbonyl-L-glutamate.

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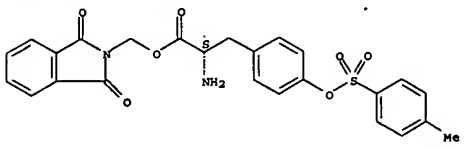
IT 889870-97-7P, Tyrosine, ester with N-(hydroxymethyl)phthalimide, p-toluenesulfonate (salt)
RL: PREP (Preparation)
(preparation of)
RN 889870-97-7 CAPLUS
CN Tyrosine, ester with N-(hydroxymethyl)phthalimide, p-toluenesulfonate (salt) (7CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:449588 CAPLUS
DOCUMENT NUMBER: 57:49588
ORIGINAL REFERENCE NO.: 57:9948c-i,9949a-i,9950a-g
TITLE: Plastein reactions. IV. Syntheses of further plastein-active pentapeptides
AUTHOR(S): Determann, Helmut; Zipp, Otmar; Wieland, Theodor
CORPORATE SOURCE: Univ. Frankfurt/Main, Frankfurt, Germany
SOURCE: Ann. (1962), 651, 172-84
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. CA 57, 6281f, 6282c. Nine pentapeptides [Tyr-Ileu-Gly-Lys-Phe (I), Tyr-Leu-Gly-Glu-Phe (II), Tyr-Leu-Gly-D-Glu-Phe (III), Tyr-Leu-Gly-Glu-Tyr (IV), Tyr-Leu-Gly-Glu(NH2)-Tyr (V), Tyr-Leu-Gly-Val-Phe (VI), Tyr-Leu-Gly-Lys-Phe (VII), Tyr-Lys-Gly-Glu-Phe (VIII), Tyr-Lys-Gly-Lys-Phe (IX)] (all amino acids have L configurations except where otherwise indicated) with aromatic end-amino acids were synthesized according to standard methods and examined as to their usefulness as plastein formers using pepsin or chymotrypsin. All gave polypeptides (plasteins) of mol. wts. 1500-4000. General procedures. Me esters. MeOH (70 cc.) cooled as low as possible in an ice-salt mixture, treated with 8 cc. SOCl2, treated with 0.1 mole amino acid at room temperature, kept 1-2 hrs. at room temperature, refluxed 30-60 min., concentrated in vacuo, and the mixts. diluted with Et2O gave 80-90% Me ester HCl salt. Benzyl esters. The amino acid or dipeptide (1 equivalent) ground with 1.2 equivs. p-MeC6H4SO3H (X), the mixture made into a paste with 5-10 equivs. PhCH2OH (XI), rinsed into a flask with 8-10 times its weight C6H6, refluxed 2-3 hrs. under a H2O separator by means of a boiling H2O bath, cooled, after 2 hrs. the precipitate filtered off, washed with Et2O, and recrystd. from tetrahydrofuran gave 70-80% tosylate of the benzyl ester. Peptide syntheses via mixed anhydrides. (a) With amts. up to 0.01 mole. The carbobenzoxyamino acid (I equivalent) and 2 equivs. Et3N dissolved in dry tetrahydrofuran (50 cc./0.01 mole) cooled in an ice-salt mixture in a flask closed with a ground-glass stopper, after 5 min. the solution treated dropwise with 1 equivalent ClCO2Et (XIII) [with very small samples (>0.001 mole) it was diluted with tetrahydrofuran] with shaking, the flask closed, kept 20 min. in the cooling mixture with occasional shaking, after formation of the mixed anhydride the mixture cooled to 0°, treated in 1 lot with 1 equivalent salt of the ester component in a little H2O or tetrahydrofuran-H2O at 0°, the flask shaken until warm to the hand (the stopper was lifted occasionally to allow CO2 to escape), the mixture concentrated in vacuo, the residue taken up in a convenient volume EtOAc, the solution washed with 5% aqueous NaHCO3, H2O, N HCl, and H2O until neutral, dried, concentrated in vacuo, and diluted with petr. ether gave the peptide; in the event the product separated as a solid which was difficultly soluble in EtOAc, it was washed as above by grinding in a mortar and filtering. (b)

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Larger amts. The carbobenzoxyamino acid (1 equiv.) and 2 equivs. Et3N in tetrahydrofuran cooled to -15° in an ice-salt mixt., the soln. treated with 1 equiv. XII at below -4° with stirring, the mixt. stirred 30 min. at below -4°, treated in 1 lot with a precooled aq. soln. (if necessary it also contained tetrahydrofuran) of 1 equiv. salt of ester component with stirring, the cooling bath removed, the whole stirred 1-2 hrs. until it attained room temp., and worked up as above gave the peptide. Peptide synthesis with dicyclohexylcarbodiimide (XIII). The acid component (1 equiv.) and 1 equiv. Et3N in tetrahydrofuran (30 cc./0.01 mole) cooled to -15°, the soln. treated with precooled (-15°) solns. of 1 equiv. ester HCl salt (or HBr salt) in tetrahydrofuran and 1.1 equivs. XIII in tetrahydrofuran (with salts, some H2O was required) in the sequence stated followed by addn. of the basic component (if this existed as the tosylate, the free base was prepd. from it: 1 equiv. tosylate and 3 equivs. K2CO3 ground intimately, suspended in EtOAc, covered with H2O, the whole shaken until soln. occurred, the EtOAc layer washed rapidly twice with H2O, dried briefly, concd. in vacuo at 30°, the residue taken up in tetrahydrofuran, and the soln. of the free base used immediately), the whole kept 1 hr. at -15°, 1 day at 0°, and 1-2 days at room temp. with occasional shaking, the excess XIII destroyed with several drops AcOH, the mixt. kept 1 hr., filtered, and the filtrate worked up as above gave the peptide. Ester sapon. The acylpeptide ester (1 equiv.) dissolved or suspended in Me2CO (150 cc./0.01 mole) treated with 1.2 equivs. N NaOH (when tyrosine was present 2.2 equivs. NaOH were required) with vigorous stirring (vibromixer) (after 10 min. a part of the expected acid pptd. as a gelstinous Na salt and this was dissolved by adding H2O), the soln. stirred 1.5 hrs. while adding H2O to effect soln., the Me2CO removed in vacuo, and the alk. soln. extd. with EtOAc gave the acid as its Na salt; if the Na salt was obtained as a gelatinous ppt., the aq. soln. was acidified with 2N HCl, extd. with EtOAc, the ext. washed with H2O, dried, concd. in vacuo, and dild. with petr. ether to give the free acid. Hydrogenolysis. The carbobenzoxypentapeptide benzyl ester in abs. AcOH contg. Pd black hydrogenated at 40° with stirring (vibromixer) (the AcOH must be free from Ac2O, as detd. by a neg. result with the hydroxamic acid reaction) [with more plentiful application of catalyst (proportion by wt. to 1:1), the reaction was completed after 2-4 hrs.], filtered, the filtrate concd. in vacuo, and dild. with abs. Et2O gave the free pentapeptide. Carbobenzoxypeptide Me esters in abs. MeOH (50 cc./0.01 mole) treated with 2-3 equivs. HCl in MeOH and Pd black, hydrogenated 1 hr. at 40° while vibrating, filtered, the filtrate evapd. in vacuo, and the residue treated with dry MeOH followed by abs. Et2O gave the peptide Me ester HCl salt. Cleavage of the carbobenzoxy group with AcOHHBr. The finely powd. carbobenzoxy compd. covered with a 20% soln. of dry HBr in abs. AcOH (1 cc./millimole), shaken 20 min. excluding moiature, the soln. dild. with abs. Et2O, stirred several min., the Et2O layer decanted from sepd. oil, and the oil digested 5-6 times with fresh Et2O gave the product as the HBr salt. Redn. with Na in liquid NH3. The protected peptide in liquid NH3 (200 cc./0.01 mole) treated portionwise with Na (6 g.-atoms/1 mole tosyl group to be cleaved or 2 g.-atoms for carbobenzoxy or benzyl ester groups) with vigorous stirring, when the blue color persisted for 3 min. the color discharged by addn. of cation

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exchange resin, 20 g. dried (at 70°) Dowex 50 X-4 (NH4+ form)/1 g. Na, the mixt. stirred until the NH3 had evapd., the residue kept 12 hrs. in vacuo over concd. H2SO4, extd. with a large vol. H2O, the ext. neutralized with AcOH, concd. in vacuo to very small vol., and treated with EtOH or Me2CO gave the free peptide. Countercurrent distribution. The protected peptide (1-1.5 g.) was distributed in 8:2:5:5 MeOHH2O-CHCl3-CCl4 in a Craig hand-app. according to Hecker with 37 elements (20 cc. each phase, 55 transfers). (The following abbreviations are used: Z = carbobenzoxy, Tos = p-toluenesulfonyl, OBzl = benzyl ester, OMe = Me ester). From 4.35 g. Z-ε-Tos-Lys (XIV) (Roeske, et al., CA 51, 2552h), 2.8 cc. Et3N, 0.95 cc. XII, and 2.92 g. Phe-OBzl.HCl was prepd. (anhydride method) 4.7 g. Z-ε-Tos-Lys-Phe-OBzl (XV), m. 130-1° (EtOAc-petr. ether). Treatment of 3.36 g. XV with 5 cc. 20% AcOH-HBr gave 2.56 g. ε-Tos-Lys-Phe-OBzl.HBr (XVI), m. 152-3° (MeOH-Et2O). Z-Tyr-Ileu-Gly (XVII) (CA 57, 6282c) (2.92 g.), 1.68 cc. Et3N, 0.75 cc. XII, and 3.71 g. XVI gave 2.3 g. Z-Tyr-Ileu-Gly-ε-Tos-Lys-Phe-OBzl (XVIII), m. 172-4° (iso-PrOH). XVII (1.22 g.), 0.3 cc. Et3, 1.55 g. XVI, and 510 mg. XIII gave 1.3 g. XVIII, m. 172-5° (iso-PrOH). XVII (4.85 g.), 2.8 cc. Et3N, 0.95 cc. XII, and 3.32 g. ε-Z-Lys-OMe.HCl gave 4.8 g. Z-Tyr-Ileu-Gly-ε-Z-Lys-OMe, m. 265° (tetrahydrofuran). ClCO2CH2Ph (35 cc.) and 50 cc. 4N NaOH added dropwise simultaneously during 1 hr. to 18.1 g. tyrosine in 100 cc. 2N NaOH with stirring at 5-10°, stirred 1 hr., dild. with H2O to twice the vol., extd. with Et2O, the aq. layer kept 1 hr. at room temp. with 25 cc. 4N NaOH, the soln. extd. with Et2O, and acidified gave 24.4 g. Z-Tyr (XIX), m. 100°. Z-Leu-OMe (22 g.), 25 cc. Et3N, 7.9 cc. XII, and 10.4 g. Gly-OMe.HCl (XIXa) gave 18.2 g. Z-Leu-Gly-OMe (XX), m. 93° (EtOAc-petr. ether). Hydrogenolysis of 18 g. XX gave 12.5 g. Leu-Gly-OMe.HCl (XXI), solidified foam. XIX (22 g.), 9.8 cc. Et3N, 17 g XXI, and 15.5 g. XIII gave 21 g. Z-Tyr-Leu-Gly-OMe (XXII), amorphous gel from EtOAc-petr. ether. Sapon. of 12.7 g. XXII with 40 cc. N NaOH gave 7.1 g. Z-Tyr-Leu-Gly (XXIII), m. 170° (EtOAc-petr. ether). XIV (17.4 g.), 11.2 cc. Et3N, 3.8 cc. XII, and 5.0 g. XIXa gave 14.4 g. Z-ε-Tos-Gly-OMe (XXIV), m. 165° (MeOH-Et2O). Cleavage of 2.53 g. XXIV with 5 cc. 20% AcOH-HBr gave 1.7 g. ε-Tos-Lys-Gly-OMe.HBr (XXV), m. 175-6°. Bis(carbobenzoxy)tyrosine (1.5g.), 0.93 cc. Et3N, 0.32 cc. XII, and 1.51 g. XXV gave 2.0 g. bis(Z)Tyr-ε-Tos-Lys-Gly-OMe (XXVI), m. 153-4° (MeOH). Sapon. of 7.0 g. XXVI with 19.3 cc. N NaOH gave 3.4 g. Z-Tyr-ε-Tos-Lys-Gly (XXVII), m.p. not sharp. Glu-Phe (D. and W., loc. cit.) (4.5 g.), 3.2 g. X, 15 cc. XI, and 150 cc. C6H6 gave 8.5 g. Glu-γ-OBzl-Phe-OBzl p-toluenesulfonate (XXVIII), m. 151-2° (tetrahydrofuran). Tosyl-D-pyrrolidonecarboxylic acid chloride (m. 85-90°) [from tosyl-D-glutamic acid (m. 143°) (Rudinger and Czurbova, CA 49, 3128f) and SOCl2] (1 mole) treated by the procedure described for the L,L-compd. (D. and W., loc. cit.) gave 2.9 g. Tos-D-Glu-L-Phe, m. 203° (iso-PrOH). Glu-Tyr (Rudinger, CA 49, 3126b) (2.95 g.), 2.2 g. X, 8 cc. XI, and 80 cc. C6H6 gave 3.3 g. Glu-γ-OBzl-Tyr-OBzl p-toluenesulfonate (XXIX), m. 145° (unsharp) (MeOH-Et2O). Z-Glu (2.8 g.), 1.4 cc. Et3N, 0.95 cc. XII, and 2.7 g. Tyr-OBzl in 25 cc. tetrahydrofuran gave 3.7 g. Z-Glu-Tyr-OBzl (XXX), m. 174-5° (MeOH). XXX (5.4 g.) cleaved with 5 cc. 20% AcOH-HBr, the resulting oily HBr salt treated with aq. K2CO3 and EtOAc, the EtOAc layer washed with H2O, dried, evapd. in vacuo at 30°, the oily residue taken up in a little

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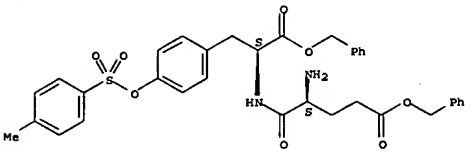
CHCl3, the soln. dild. with Et2O, and treated with HCl gave 2.3 g. Glu-Tyr-OBzl.HCl (XXXI), m. 70-2° (MeOH-Et2O). Z-Val (2.5 g.), 2.8 cc. Et3N, 0.95 cc. XII, and Phe-OMe.HCl gave 2.9 g. Z-Val-Phe-OMe (XXXII), m. 136° (MeOH). Hydrogenolysis of 4.1 g. XXXII in 5 cc. 5N MeOH-HCl gave 2.9 g. Val-Phe-OMe.HCl (XXXIII), m. 196° (MeOH-Et2O). XXIII (3.4 g.), 1.55 g. XIII, and 4.9 g. free base from 4.9 g. XXVIII gave 4.6 g. crude Z-Tyr-Leu-Gly-Glu-γ-OBzl-Phe-OBzl (XXXIV); crude XXXIV from 4 such runs combined and subjected to countercurrent distribution gave 2.3 g. XXXIV, m. 96° (EtOAc-petr. ether). XXIII (980 mg.), 440 mg. XIII, and free base from 1.44 g. XXIX gave 1.5 g. crude product, which on countercurrent distribution yielded 800 mg. Z-Tyr-Leu-Gly-Glu-γ-OBzl-Tyr-OBzl, m. 92° (EtOAc-petr. ether). XXIII (580 mg.), 0.17 cc. Et3N, 520 mg. XXXI, and 280 mg. XIII gave 800 mg. crude Z-Tyr-Leu-Gly-Glu-Tyr-OBzl, which was subjected directly to hydrogenolysis. XXIII (1.7 g.), 1.1 g. XXXIII, 0.5 cc. Et3N, and 800 mg. XIII gave 1.2 g. crude pentapeptide ester, which was sapond. directly with 3.5 cc. N NaOH to give 900 mg. Z-Tyr-Leu-Gly-Val-Phe, m. 176-8° (EtOAc-petr ether). XXIII (970 mg.), 0.26 cc. Et3N, 1.24 g. XVI, and 440 mg. XIII gave 1.3 g. crude Z-Tyr-Leu-Gly-ε-Tos-Lys-Phe-OBzl, m.p. unsharp, which was reduced as is with Na in NH3. XXVII (3.2 g.), 0.7 cc. Et3N, 3.1 g. XVI, and 1.04 g. XIII gave 3.6 g. Z-Tyr-ε-Tos-Lys-Gly-ε-Tos-Lys-Phe-OBzl, m. 161-2° (MeOH-Et2O). XXVII (1.08 g.), the free base from 1.2 g. XXVIII, and 340 mg. XIII gave 1.5 g. Z-Tyr-ε-Tos-Lys-Gly- Glu-γ-OBzl-Phe-OBzl, m. 151-3° (EtOAc-petr. ether). Hydrogenolysis or redn. with Na in liquid NH3 of the protected peptide gave the free peptide, which was characterized by paper chromatography and by paper electrophoresis before and after hydrolysis with HCl. The syntheses were schematically illustrated.

IT 889871-53-8P, Tyrosine, N-L-α-glutamyl-, dibenzyl ester, p-toluenesulfonate (salt), L-
RL: PREP (Preparation)
(preparation of)

RN 889871-53-8 CAPLUS

CN Tyrosine, N-L-α-glutamyl-, dibenzyl ester, p-toluenesulfonate (salt), L- (7CI) (CA INDEX NAME)

Absolute stereochemistry.



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ACCESSION NUMBER: 1962:411083 CAPLUS
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ORIGINAL REFERENCE NO.: 57:2319d-i,2320a-i,2321a-i,2322a-i,2323a-h
TITLE: Peptide syntheses. III. Syntheses of arginine-containing peptides
AUTHOR(S): Gibian, Heinz; Schroeder, Eberhard
CORPORATE SOURCE: Schering A.-G., West Berlin
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AB cf. CA 55, 14321d. The following abbreviations are used: Cbo = carbobenzoxy; OMe = Me ester; OEt = Et ester; OBzl = benzyl ester; DCCI = N,N'-dicyclohexylcarbodiimide; THF = tetrahydrofuran; DMF = dimethylformamide; A = EtOH; E = Et2O; PE = petr. ether; Chlf = chloroform; Ess = EtOAc; Me = MeOH; Py = pyridine; W = H2O; and Eg = HOAc.
Di-, tri-, and tetrapeptides with N-terminal ω-nitro-L-arginine, as well as dipeptides with C-terminal ω-nitro-L-arginine in the form of derivs. protected on the α-amino and carboxyl groups were synthesized by various methods, and their optical rotations compared. Most of the N-acylpeptides obtained from these by alkaline hydrolysis, as well as several free peptides were described. ω-Nitro-D-arginine (I), its Cbo compound and its Me ester were obtained. For the synthesis of arginyl peptides O2NNHC(:NH)NH(CH2)3CH(NHCbo)CONHCHRCO2R (II), Cbo-nitro-L-arginine was used in all cases. For the formation of the peptide bond, the following methods were used: mixed anhydride, carbodiimide, phosphorazo, cyanomethyl ester, and carbonyl. All Cbo-nitro-L-arginyl-amino acid Et, Me, or benzyl esters could be obtained in average to good yields. The carbodiimide method in all cases gave the highest yields. The products obtained by the various methods showed the same rotation, so that a racemization probably did not occur. The Cbo-nitro-L-arginyl-L-amino acid Me and Et esters could be readily saponified in Me2CO-H2O solution with N NaOH. Saponification of the higher Cbo-peptide Et esters required rather long reaction times, in comparison with the dipeptide compds. Substituted ω-nitro-L-arginine peptides CboNHCHRCONHCH(CO2H)(CH2)3NHC(:NH)NHNO2 (III) had considerably less tendency to crystallize than II. Nitro-L-arginine Me ester was always used as the basic component of the coupling, since its hydrochloride (IV), in contrast to the corresponding Et ester, could readily be obtained crystalline For the coupling, the method of the mixed anhydrides or the carbodiimide method were preferred; yields of 50-90% were obtained. In contrast to the simple I derivs., some peculiarities were observed in the series of substituted III. In the decomposition of Cbo-L-glutamine the desired dipeptide derivative was not obtained by the method of mixed anhydrides, but carbethoxynitro-L-arginine Me ester (V) was obtained. This alternative cleavage of the mixed anhydride of Cbo-L-glutamine could not formerly be found with other amino acid esters. The carbodiimide method gave the dipeptide. The reaction of Cbo-L-isoglutamine with nitro-L-arginine Me ester by the anhydride method yielded 40% of the desired peptide; from the Ess solution, 20% of a higher-boiling unidentified product was isolated. The

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carbodiimide method yielded N- [γ-(Cbo-L-glutamyl)] -N, N'-dicyclohexylurea (VI). Similarly, in the prepn. of Cbo-L-glutamyl-(α-Et ester)-γ-nitro-L-arginine Me ester (VII) from the components with DCCI, the urea deriv. was formed as a side product that could not be sepd. The phosphorazo method, which gave good yields in the case of II, was less well suited for III. It gave impure products in 20-30% yields. All the Cbo-amino acid-nitro-L-arginine Me esters could be readily converted in good yields to the corresponding Cbo-dipeptide acids under the usual sapon. conditions. Some of the peptide derivs. were catalytically hydrogenated in MeOH in the presence of Ess and Pd. Characteristic examples of the prepn. of the compds. are given. D-Arginine-HCl (22.05 g.) added in small portions to a mixt. of 24.2 cc. fuming HNO3 and 19.3 cc. fuming H2SO4 (25%SO3) at 0.5°, 9.3 cc. concd. H2SO4 added, and the mixt. stirred 1 hr., poured onto ice, brought to pH 8 with concd. NH4OH, allowed to stand several hrs., and then brought to pH 6 with 5N Eg gave 53% I, m. 253-4° (H2O), [α]22D -22.6° (c 1, 2N HCl). Nitro-L-arginine was similarly prepd. in 53-79% yield. I (8.76 g.) in 20 cc. 2N NaOH treated at 0° with 8.2 g. carbobenzoxy chloride and 4N NaOH, and the mixt. stirred 2-3 hrs. at room temp. gave 68% Cbo-nitro-D-arginine, m. 132-4° (A-H2O), [α]23D 2.8 (2, MeOH). The corresponding L-compd. was similarly prepd. in 60-95% yield. I (4.95 g.) warmed to 40° for 4 hrs. with 1.96 cc. SOCl2 and 40 cc. MeOH and the soln. kept 20 hrs. at room temp. gave 74% nitro-D-arginine Me ester-HCl, m. 154-6° (abs. MeOH-abs. E), [α]23D -14.7° (c 2, MeOH).
IV was similarly prepd. in 92% yield. The prepn. of the amino acid benzyl esters benzenesulfonates is illustrated by the following examples. L-Leucine (39.8 g.), 180 cc. benzyl alcohol, 52.2 g. benzenesulfonic acid, and 100 cc. C6H6 were heated 3-4 hrs. with slow distn. of H2O and C6H6 to form 75% L-leucine benzyl ester benzenesulfonate, m. 167-8° (A-E), needles, [α]21D 4.4° (c 2, DMF). L-Tyrosine benzyl ester benzenesulfonate was similarly prepd. in 70% yield, m. 143-5° (A-E), [α]23D -3.8° (c 2, DMF). D-Aspartic acid dibenzyl ester toluenesulfonate was similarly prepd. in 92% yield from 3.93 g. D-aspartic acid, 6.27 g. p-toluenesulfonic acid-H2O, 36 cc. benzyl alc., and C6H6 [needles, m. 156-8° (A-E), [α]23D -7.4° (c 2, Chlf)]. L-Alanine benzyl ester totuenesulfonate, needles, m. 116-18° (A-E), [α]26D -6.0° (c 4, abs. MeOH), and L-valine benzyl ester toluenesulfonate were similarly prepd. in 84 and 68% yields, resp. The following examples of the prepn. of II are given. Anhydride method: Cbo-nitro-L-arginine (3.53 g.) in 10 cc. THF, and 1.39 cc. Et3N treated with 0.95 cc. EtO2CCl at 10° the mixt. kept 10 min. at -5°, 4.55 g. L,-valine benzyl ester toluenesulfonate in 10 cc. THF and 1.67 cc. Et3N added, and the soln. slowly brought to room temp. gave 58% Cbo-nitro-L-arginyl-L-valine benzyl ester, m. 148-50° (A-H2O), plates, [α]28D -23.1° (c 2, dioxane).
Carbodiimide method: 1.31 g. *S*-benzyl-L-cysteine Me ester-HCl in 2-4 cc. DMF treated with 0.84 cc. Et3N and 5 cc. THF, the suspension quickly cooled, the Et3N.HCl removed by suction, the mixt. united with a soln. of 1.77 g. Cbo-nitro-L-arginine in 5 cc. THF, and kept 24 hrs. at room temp.

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room temp. gave 28% N-[γ-(Cbo-L-glutaminyl)]-N,N'-dicyclohexylurea, m. 152-4° (A-H2O), [α]28D 5.7° (c 1, DMF). From the HCl ext. 0.34 g. of an unidentified substance, m. 190-7°, [α]28D 2.4° (c 1, DMF) was obtained. Carbodiimide method: The dicyclohexylamine salt of Cbo-L-glutamic acid α-Et ester (4.9 g.) in 30 cc. DMF and 2.7 g. nitro-L-arginine Me ester-HCl in 5 cc. DMF at room temp. were treated with 2.47 g. DCCI; the mixt. was held 24 hrs. at room temp.; 4.94 g. VII contaminated with N-[γ-(Cbo-L-glu-α-OEt)]-N,N'-dicyclohexylurea was obtained, m. 90-5°. The mixt. (0.79 g.) was hydrolyzed 1 hr. with N NaOH in 6 cc. 1:1 Me2CO-H2O; 0.44 g. N-[γ-(Cbo-L-glutamyl)]-N,N'-dicyclohexylurea, needles, m. 150-1° (Eg-PE), was obtained. Similar hydrolysis of 0.47 g. Cbo-L-valyl-nitro-L-arginine Me ester gave 93% Cbo-L-valyl-nitro-L-arginine, plates, m. 175-7° (A-H2O), [α]28D -9.3° (c 1, A). Hydrogenolytic removal of the protective group was carried out as follows. Cbo-nitro-L-arginyl-L-valine benzyl ester (1.63 g.) in 18 cc. MeOH, 3 cc. Eg, and 3 cc. H2O was hydrogenated with Pd to give 95% L-arginyl-L-valine acetate, m. 213-15°, [α]23D 12.0° (c 1, H2O). The following II were prepd. (dipeptide, where R = Cbo-nitro-L-Arg-; method(s) and yield(s); cryst. form, crystn. solvent, and m.p. (if not previously reported in the literature); and [α]D by the method and at the temp. specified given): R-L-Ala-OBzl, anhydride method in THF, 62%, -, -19.1° (c 2, dioxane, 30°); R-L-Ala-OMe, anhydride method in THF, 49%, -, -19.9° (c 1, Me, 24°); R-nitro-L-Arg-OMe, anhydride method in THF-DMF, 36% (a), DCCI in THF-CH2Cl2-DMF, 44% (b), amorphous from Me-A, 145-7° (a) -9.1° (c 1, DMF, 25), (b) -9.0° (c 1, DMF, 30°); R-L-Asp-(OEt)2, anhydride method in THF, 65% (a), DCCI in THF, 84% (b), PCl, 65% (c), - , (a) -11.6° (c 1, Me, 23°), (b) -11.6°(25°),(c) -11.7°; R-L-Asp-(OBzl)2, anhydride method in THF, 68% (a), DCCI in THF, 86% (b), -, (a) -4.9° (c 2, Me-dioxane, 22°), (b) -5.0° (23°); R-S-Bzl-L-Cys-OMe, anhydride method in THF-DMF, 65% (a), DCCI in THF-DMF, 71% (b), 153.5-154.5°, needles, Ess, Ess-PE, or A-W, (a) -37.3° (c 1, Me, 23°), (b) -37.4° (23°); R-S-Bzl-L-Cys-OBzl, anhydride method in THF, 43% (a), DCCI in THF, 65% (b), 151-2°, needles, A-W, (a) -42.4° (c 1, dioxane, 22°), (b) -41.5° (23°); R-L-Glu-(OBzl)2, anhydride method in THF, 65% (a), DCCI in THF, 76% (b), -, (a) -10.5° (c 1, Eg, 23°), -19.6° (c 1, Me, 24°), (b) -19.6° (24°); R-Gly-OEt, anhydride method in Chlf, 27% (a), in THF, 48% (b), DCCI in THF-Chlf, 65% (c), PCl3, 62% (d), cyano Me ester, 30% (e), carbonyl, 40% (f), 77-8° or 118-20°, needles, Ess-PE or A-W, (a) -15.8° (c 2, Me, 22°, (b) -14.6° (25°), (c) -15.0° (23°), (d) -14.3° (27°), (e) -13.7° (25°), (f) -13.4° (27°); R-Gly-OBzl, anhydride method in Chlf, 16% (a), in THF, 50% (b), DCCI in THF, 57% (c), -, (b) -14.3° (c 2, Me, 25°), (c) -13.4° (24°); R-L-LeM-OMe, anhydride method in Chlf, 27% (a), in THF, 42% (b), DCCI in DMF-THF-Chlf, 72% (c), PCl3, 62% (d), (a) -22.3° (c 1, Me, 22°), (b) -23.2° (25°), (c) -23.0° (24°), (d) -22.1° (23°); R-L-Leu-OBzl, anhydride method in THF, 55% (a), DCCI in THF, 85% (b), -, (a) -29.5° (c 1, Me, 25°), (b) -28.5° (24°); R-α-Cbo-L-Lys-OMe, anhydride method in THF-DMF, 35% (crude 69%), 86-8°, amorphous, Ess-PE, -4.6° (c 1, dioxane, 30°); R-α-Cbo-L-Lys-OBzl, anhydride method in THF-DMF, 31% (crude 70%)

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after addn. of DCCI, 5N Eg added, the mixt. kept 1 hr. at room temp. and 1 hr. at 0°, and the N,N'-dicyclohexyl urea filtered off gave 71% Cbo-nitro-L-arginyl-S-benzyl-L-cysteine Me ester, needles, m. 153.5-4° (A-H2O), [α]23D -37.4° (c 1, MeOH).
Phosphorazo method: 0.91 g. L-leucine Me ester HCl in 7 cc. Py treated at 0° with 0.224 cc. PCl3 in 2.8 cc. Py, after 30 min. at room temp. 1.77 g. Cbo-nitro-L-arginine added, and the mixt. kept 60 hrs. at room temp. gave 62% Cbo-nitro,-L-arginyl-L-leucine Me ester, plates, m. 160-1° (MeOH-H2O), [α]23D -22.1° (c 0.94, MeOh).
Carbonyl method: 3.53 g. Cbo-nitro-L-arginine and 1.29 g. carbonylglycine Et ester in 2 cc. abs. Py kept 15 min. at room temp. and then warmed 1 hr. to 60° gave 400% Cbo-nitro-L-arginyl-glycine Et ester, m. 118-20° (A-H2O), [α]27D -13.4° (c 2, MeOH).
Cbo-nitro-L-arginyl-L-valine Me ester (0.47 g.) in 5 cc. 1:1 Me2CO-H2O stirred 1.5 hrs. with 1.1 cc. N NaOH at room temp. gave 71% Cbo-nitro-L-arginyl-L-valine, m. 179-9.5° (A-H2O), [α]28D -30° (c 2, A). Cbo-nitro-L-arginine (0.89 g.) in 3 cc. THF, 1 cc. DMF, and 0.35 cc. Et3N stirred at -5° with 0.24 cc. EtO2CCl for 15 min., and the mixt., after addn. of 0.003 mole L-Leu-L-Val-L-Glu-(OEt)2 (from the hydrochloride with Et3N), in 3 cc. DMF and 3 cc. THF, slowly warmed to room temp. gave 67%, Cbo-nitro-L-arginyl-L-leucyl-L-valyl-L-glutamic acid di-Et ester, m. 182-4° (A-H2O), [α]24D -20.2° (c 1, DMF). Cbo-nitro-L-Arg-L-Ala (1.06 g.) m 3 cc. DMF and 0.003 mole L-Leu-L-Val-L-Glu-(OEt)2 (from the hydrochloride and Et3N) in 6 cc. DMF treated with 0.62 g. DCCI in a small amt. of DMF, the mixt. kept 24 hrs. at room temp., excess DCCI destroyed with 5N Eg, and the urea filtered off gave 45% Cbo-nitro-L-Arg-L-Ala-L-Leu-L-Val-L-Glu acid di-Et ester, m. 199-202° (Eg-E), [α]20D -21.0° (c 0.5, DMF).
The following are examples of the methods used for the prepn. of III. Carbodiimide method: IV (1.63 g.) dissolved in 4 cc. DMF by warming, 0.84 cc. Et3N and 4 cc. CH2Cl2, and then 1.4 g. Cbo-L-glutamine in 5 cc. THF and 1.23 g. DCCI added, the mixt. kept 24 hrs. at room temp., and the excess DCCI destroyed with 5N Eg gave 52% Cbo-L-glutaminyl-nitro-L-arginine Me ester, needles, m. 166-7.5° (H2O). Et3N (0.69 cc.) and 0.48 cc. EtO2CCl added at 5° to 1.45 g. Cbo-L-glutamine (VIII) in 5 cc. THF, the mixt. stirred 10 min. at 5°, nitro-L-arginine Me ester (from 1.63 g. hydrochloride in DMF-THF with Et3N) added, and the mixt. slowly warmed to room temp. gave a compd., m. 128-30°, which analyzed as V. IV (1.35 g.) in 10 cc. Chlf and 10 cc. N NaOH stirred with 0.52 cc. EtO2CCl 15 min. at 0° and 30 min. at room temp. gave 0.8 g. V, m. 130-1° (H2O). Anhydride method: Cbo-L-isoglutamine (1.4 g.) in 5 cc. THF, 1 cc. DMF, and 0.69 cc. Et3N treated at -5° with 0.48 cc. EtO2CCl, the mixt. stirred 10 min. at -5°, nitro-L-arginine Me ester (from 1.63 g. IV and Et3N) in 3 cc. DMF and 5 cc. CH2Cl2 added, and the mixt. slowly warmed to room temp. gave 40% Cbo-L-isoglutaminyl-nitro-L-arginine Me ester, m. 155-6° (H2O), [α]28D -2.0° (c 1, DMF); when the HCl ext. obtained in this prepn. was kept a long time, 0.5 g. of an unknown substance, m. 196-7.5° (H2O), was obtained. VIII (0.8 g.) in 5 cc. THF, 1 cc. DMF, and nitro-L-arginine Me ester (from 1.09 g. hydrochloride and Et3N) in 3 cc. DMF and 3 cc. CH2Cl2 treated with 0.73 g. DCCI for 24 hrs. at

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(a), DCCI in THF-DMF, 69% (b), 137.5-138.5°, -, Ess-PE or A-W, (a) -11.4° (c 2, dioxane, 28°), (b) -11.8° (28°); R-L-Phe-OMe, anhydride method in THF-DMF, 50%, -, -8.6° (c 1, Me, 24°); R-L-Pro-OBzl, DCCI in THF-CH2CL2-DMF, 78%, 146-7°, needles, A-W or Ess-PE, -50.6° (c 2, Me, 27°); R-L-Pro-OMe, DCCI in THF-DMF, 61%, 159-60°, plates, A-W or Ess-PE, -53.0° (c 2, Me, 27°); R-L-Tyr-OEt, anhydride method in Chlf, 43% (a), in THF, 66% (b), DCCI in THF, 73% (c), -, (b) -6° (c 3, Me, 22°), (c) -5° (c 4, Me, 22°); R-L-Tyr-OBzl, anhydride method in THF, 54% (a), DCCI in THF, 54% (b), -, (a) -13.2° (c 1, A, 25°); R-L-Val-OBzl, anhydride method in THF, 58%, 148-50°, plates, A-W or Ess-PE, -27.5° (c 1, Me, 23°), 23.1° (c 2, dioxane, 28°); R-L-Val-OMe, anhydride method in THF-DMF, 57%, -, -14.6° (c 2, dioxane, 28°); Cbonitro-D-Arg-D-Asp-(OBzl)2, DCCI in THF, 77%, 109-10°, plates, A-W, 3.5° (c 2, Me-dioxane, 23°); and Cbo-nitro-L-Arg-D-Ser-OMe, anhydride method in THF-DMF, 13%, 172-3.5°, -, A-E, PE, -8.0° (c 0.5, A, 23°). The following Cbo-nitro-L-arginyl amino acids were prepd. (peptide, where R = Cbo-nitro-L-Ar-; yield; m.p., cryst. form, and crystn. solvent (if not previously recorded in the literature); and [α]D at the temp. specified given): R-L-Ala-OH, 91%, -, -6.3° (c 1, Py, 30°), -5.9 (c 1.8, Py, 29°); R-nitro-L-Arg-OH, 83%, 176-8°, plates, Eg-E, 2.3° (c 2, DMF, 24°); R-S-Bzl-L-Cys-OH, 88% (crude), 181-2°, small rods, A-W, -27.2° R-Gly-OH, 88%,-, -15.2° (c 1, Me, 23°); R-L-Leu-OH, 92%, -, -5.7° (c 3.4, Py, 24°); R-α-Cbo-L-Lys-OH, 81% (crude), 161-3°, cryst., A-W, 4.4° (c 1, A, 30°); R-L-Phe-OH, 98% (crude), -, 12.5° (c 1, Py, 23°); R-L-Pro-OH.THF, 76%, 124-6°, prisms, THF-PE, -28.8° (c 1, DMF, 26°); R-L-Tyr-OH, 98% (crude), -, 17.3° (c 2, Py, 23°); and R-L-Val-OH, 75% (crude), 179-9.5°, thick crystals, A-W, -2.9° (c 2, A, 28°). The following higher arginine peptides were prepd., predominantly according to the anhydride method (peptide (R = Cbo-nitro-L-Arg-); starting material; yield; m.p.; crystn. form; crystn. solvent; [α]D at the temp. specified given): R-L-Ala-L-Leu-L-Val-L-Glu-(OEt)2, R-L-Ala-OH, 45%, 199-202°, amorphous, Eg-E, -21.0° (c 5, DMF, 20°); R-L-Leu-L-Glu(OBzt)2, R-L-Leu-OH, 74%, 117-19°, platelets, A-W, -8.7° (c 0.5, DMF, 24°); R-L-Leu-L-Leu-OEt, R-OH, 51%, 107-9°, platelets, A-W, -31.4° (c 1, A, 27°); R-L-Leu-L-Leu-L-Leu-OEt, R-L-Leu-OH, 60%, 138-40°, needles, A-W, -43.8° (c 1, A, 27°); R-L-Leu-L-Val-L-Glu-(OEt)2, R-OH, 67%, 182-4°, fine crystals, A-W or Ess-PE, -20.2° (c 1, DMF, 24°); R-L-Leu-L-Glu-(OEt)2, R-L-Leu-OH, 79%, 124-6°, platelets, A-W, -; R-L-Val-L-Leu-OBzl, R-L-Val-OH, 81%, 91-8°, crystals, A-W, -13.5° (c 1, DMF, 20°); Cbo-L-Leu-nitro-L-Arg-L-Leu-L-Leu-OEt, Cbo-L-Leu-nitro-L-Arg-OH, 32%, 169-70°, needles, A-W, -37.7° (c 1, A, 30°); and Cbo-L-Ala-nitro-L-Arg-L-Asp-(OBzl)2, Cbo-L-Ala-nitro-L-Arg-OH, 73%, 104-8°, crystals, Ess-PE, -15.2° (c 1, DMF, 20°).
The following III were prepd. (peptide (R = -nitro-L-Arg-OMe), method(s) and yield(s), m.p., cryst. form, and crystn. solvent (if not previously reported in the literature, or if the compd. has previously been obtained only as an oil), and [α]D at the temp. specified given): Cbo-L-Ala-R, anhydride method in DMF-CH2Cl2, 89%, 121-2°, granular powder, Ess-PE, -; Cbo-L-Asp-(β-OMe)-R, anhydride method, THF-DMF-CH2Cl2, 68%, 112-13°, needles, Ess-PE, -11.5° (c 1, A, 28°); Cbo-L-Asp-(β-OBzl)-R, anhydride method in

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THF-DMF-CH2Cl2, 71% (a), DCCI in THF-DMF-CH2Cl2, 75% (b), 108-10°, needles, A-W or Ess-PE, (a) -8.7° (c 3, dioxane, 23°), (b) -9.6° (23°); Cbo-S-Bzl-L-Cys-R, anhydride method in THF-DMF-CH2Cl2, 61% (a), DCCI in THF-DMF-CH2Cl2, 79% (b), PCl3, 46% (c), cyano Me ester, 45%, (d), 88-9°, needles, isopropyl alc.-A, (a) -24.2° (c 1, A, 25°), (b) -24.8° (25°), (c) -23.5 (30°), (d) -23.0° (30°); Cbo-L-Glu-(γ-OBzl)-R, DCCI in THF-DMF-CH2Cl2, 93%, 80-90°, amorphous, Ess-PE, -7° (c 2, A, 25°); Cbo-L-Glu-(γ-NH2)-R, DCCI in THF-DMF-CH2Cl2, 52%, 166-7.5°, fine needles, W or A-W, or Me-E, -; Cbo-L-Glu-(α-NH2)-R, anhydride method in THF-DMF-CH2Cl2, 40%, 155-6°, crystn., W, -2.0° (c 1, DMF, 26°); Cbo-L-Glu-(α OEt)-R, anhydride method in THF-DMF-CH2Cl2, 77%, 74-8°, amorphous, Ess-PE, -15.8° (c 2, A, 25°); Cbo-Gly-R, anhydride method in THF-DMF, 45% (a), DCCI, 31% (b), PCl3, 29% (crude) (c), cyano Me ester, 34% (d), azide, 45% (crude) (e), 110-12°, platelets, Ess-PE, (a) -14.7 (c 2, Me, 22°), (b) -13.7° (22°), (c) -13.3° (22°), (d) -14.3° (23°), (e) -14.6° (22°); Cbo-L-Leu-R, anhydride method in THF-DMF-CH2Cl2, 90% (a), DCCI in THF-DMF-CH2Cl2, 100% (b), oil, (a) -20.0° (c 2, A, 23°), (b) -20.2° (22°); α,ε-di-Cbo-L-Lys-R, anhydride method in THF-CH2Cl2, 66%, -, -11.4° (c 3, Me, 24°); α-Cbo-ε-tosyl-L-Lys-R, DCCI in THF-DMF-CH2Cl2, 81%, 141-3°, needles, Ess-PE, -12.0° (c 2, dioxane, 22°); Cbo-L-Pro-R, anhydride method in THF-DMF-CH2Cl2, 78% (a), PCl3, 26% (b), oil, (a) -43.3° (c 2, Me, 23°), (b) -45.2° (25°); Cbo-L-Tyr-R, anhydride method in THF-DMF-CH2Cl2, 50% (a), DCCI in THF-DMF-CH2Cl2, 92% (b), PCl3, 24% (c), Azide, 61% (d), 170-1°, needles, Ess-PE, (a) -11.1° (c 2, A, 22°), (b) -12.0° (23°), (c) -7.7° (24°), (d) -9.8° (22°); Cbo-L-Val-R, anhydride method in THF-DMF-CH2Cl2, 76%, 162-2.5°, needles, A-W or Ess-PE, -26.8° (c 2, dioxane, 28°); Cbo-L-Ser-R, azide method, 24%, anhydride method, 29%, oil, -; and Cbo-D-Val-nitro-D-Arg-OMe, anhydride method in THF-DMF, 69%, 159.5-61°, needles, A, -26.1° (c 1, dioxane, 23°). The following Cbo-amino acid-nitro-L-arginine compds. were prepd. from the corresponding esters by sapon. with N NaOH in aq. Me2CO (peptide where R = -nitro-L-Arg-OH; yield; m.p., cryst. form, and crystn. solvent (if not previously reported in the literature); and [α]D at the temp. specified given): Cbo-L-Ala-R, 76%, 168-70°, -, A-W, -9.9° (c 2, Me, 25°); Cbo-L-Glu-(γ-OBzl)-R, 40% (crude), 153-5°, platelets, A-W, 0° (c 1, A, 28°); Cbo-L-Glu-(α-NH2)-R, 73%, 216-17°, -, DMF-W, -; Cbo-Gly-R, 60%, 143-5°, platelets, A-W, 2.8° (c 2, Eg, 24°); Cbo-L-Leu-R, 81%, 161-4°, needles, A-W, -10.8° (c 2, Eg, 24°); α-CbO-ε-tosyl-L-Lys-R, 98% (crude), does not m. sharply, amorphous, -, -6.4 (c 2, Py, 22°); Cbo-L-Pro-R, 79% (crude), does not m. sharply, needles, A-W, -33.2° (c 4, Me, 24°); Cbo-L-Tyr-R, 97%, 165-8°, -, A-W, 3.8° (c 3, Py, 23°); Cbo-L-Val-R, 93% (crude), 175-7°, platelets, AOW, -9.8° (c 1, A, 28°); and Cbo-D-Val-nitro-D-Arg-OH, 72%, 173-5°, platelets, A-W, 8.0° (c 1, A, 23°). The following free peptides were prepd. by

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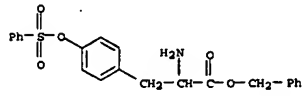
hydrogenolysis of the derivs. in a mixt. of M-Eg-H2O with H over Pd (peptide; yield; m.p., cryst. form, and crystn. solvent (if not already reported in the literature); and [α]D at the temp. specified given): L-Arg-L-Ala acetate, 58%, -, 10.4° (c 2, W, 27°); L-Arg-L-Asp.H2O, 78%, -, 24.1° (c 2, W, 29°); L-Arg-L-Glu.0.5H2O, 64%, -, 24.2° (c 1, W, 25°); L-Arg-L-Lys diacetate, 75% (crude), 80-1°, -, W-A, Ess, 14.2° (c 1, W, 23°); L-Arg-L-Phe acetate, 61%, -, 29.0° (c 1, W, 22°); L-Arg-L-Val acetate, 95%, 213-17°, platelets, W-A, Ess, 12.3° (c 2, W, 25°); L-Arg-L-Leu-L-Glu, 78%, -, -, A-W, -0.4° (c 0.5, W, 20°); L-Ala-L-Arg-L-Pro acetate (from Cbo-L-Ala-nitro-L-Arg- L-Pro-OBzl), -, -, -; L-Ala-L-Arg-L-Asp, -, -, -1.6° (c 0.5, W, 21°); L,-Arg-L-Val-L-Leu acetate, 80%, -, -11.0° (c 0.5, W, 20°); L-Glu-L-Arg.0.5H2O, 93%, 238-9°, platelets, W-A, -; L-Glu-(α-NH2)-L-Arg acetate, 100%, hygroscopic, not cryst., -; L-Pro-L-Arg acetate, 84%, 183-4°, platelets, W-A, -26.9° (c 1, W, 30°); and D-Arg-D-Asp, 89%, platelets, W-A, -24.5° (c 1, W, 23°).

IT 95130-89-5P, Tyrosine, benzyl ester, benzenesulfonate
RL: PREP (Preparation)
(preparation of)

RN 95130-89-5 CAPLUS

CN Tyrosine, benzyl ester, benzenesulfonate (7CI) (CA INDEX NAME)



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AB New polyiodo acids useful as potential contrast agents in radiology are described. 4-HOC6H4COCHO (I) (2.4 g.) in a little warm EtOH was treated with 3,4-(H2N)2C6H3CO2H.HCl (II) (2.7 g.) and the mixture warmed 1 hr. on the water bath to give 2-(4-hydroxyphenyl)quinoxaline-6-carboxylic acid (III), m. 300-5° (dilute EtOH). III (2.66 g.) in AcOH was treated by warming with ICl (4.83 g.) in HCl, the mixture after standing overnight was diluted and filtered, and the precipitate washed with H2O and dilute solution of Na2S2O3 to give a crude product, which was purified by dissolving in NaOH and precipitating with HCl to obtain 2-(3,5-diiodo-4-hydroxyphenyl)quinoxaline-6-carboxylic acid (IV), m. 267-9°. Similar treatment of 3,4,6-(H2N)2(HO)C6H2CO2H.HCl (V) in H2O with I gave the 7-hydroxy derivative (VI) of III, m. 278-80° (decomposition), which was iodinated as above with ICl to give the 7-hydroxy derivative (VII) of IV, m. 345°. Oxidation with KMnO4 of IV and VII gave 3,5-diiodo-4-hydroxybenzoic acid, m. 240°. An aqueous solution of 3-O2NC6H4COCHO (VIII) (prepared from 4.5 g. of 3-O2NC6-H4Ac in EtOH by oxidation with SeO2) treated with an aqueous solution of 1,2-(H2N)2C6H4 gave 2-(3-nitrophenyl)quinoxaline (IX), m. 182-3° (EtOH), while the aqueous solution of VIII treated with excess of II in H2O gave a precipitate which was purified by dissolving in dilute NH4OH and precipitating with dilute HCl to give 2-(3-nitrophenyl)quinoxaline-6-carboxylic acid (X), m. 290-2° (AcOH). Reduction of X with SnCl2 in concentrated HCl gave 2-(3-aminophenyl)quinoxaline-6-carboxylic acid hydrochloride (XI) from whose aqueous solution by treating with AcONa the free base (XII), m. 275-6° (decomposition), was obtained. XII (0.3 g.) treated with ICl (0.6 g.) in dilute HCl gave 2-(4,6-diiodo-3-aminophenyl)quinoxaline-6-carboxylic acid (XIII), m. 320° (decomposition). L-Tyrosine (4 g.) was dissolved in a solution of 2.65 g. NaOH in 100 ml. H2O and treated portionwise with stirring with 5.16 g. 4-AcNHC6H4SO2Cl (XIV), the mixture filtered, and the filtrate acidified with HCl to give N,O-bis(acetylsulfanilyl)tyrosine (XV), m. 245-8° (dilute EtOH). XV (1 g.) was refluxed 30 min. with 10 ml. dilute HCl and the mixture cooled and neutralized with Na2CO3 to give α-sulfanilamido-β-(4-hydroxyphenyl)propionic acid (XVI), m. 125° (dilute EtOH), which treated with ICl in AcOH gave α-sulfanilamido-β-(3,5-diiodo-4-hydroxyphenyl)propionic acid (XVII), m. 160°. 3,5-Diiodo-L-tyrosine (0.48 g.) was dissolved in H2O by addition of 3 ml. N KOH, treated with stirring with 3 g. XIV and acidified after standing overnight with dilute HCl to give α-acetylsulfanilamido-β-(3,5-diiodo-4-

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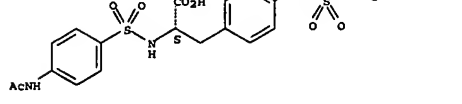
hydroxyphenyl)propionic acid (XVIII), m. 177-80°, which on hydrolysis with dil. HCl gave XVII. 4-BzOC6H4COCH2Br (XIX) (3.2 g.) (prepd. in 90% yield from 4-BzOC6H4Ac on bromination in CHCl3 under ultraviolet light) dissolved on warming in a little EtOH was treated with 2.74 g. 4-H2NC6H4CO2H (XX) in EtOH to give 4-(4-benzoyloxyphenacylamino)benzoic acid (XXI), m. 235-7° (decompn.) (Me2CO), which on recrystn. from AcOH gave 4-(4-acetoxyphenacylamino)benzoic acid (XXII), m. 225-7°. By refluxing 6 g. XXI in 100 ml. 10% NaOH, cooling, and acidifying with dil. HCl 4-(4-hydroxyphenacylamino)benzoic acid (XXIII), m. 265° (decompn.) (EtOH), was obtained. XIX (6.60 g.) in EtOH was refluxed with 4-HN2-C6H4CO2Et (6.40 g.) to give Et 4-(4-benzoyloxyphenacylamino)benzoate (XXIV), m. 184-6° (C6H6) which on hydrolysis with 5% NaOH gave XXIII. On treatment of XXIII in AcOH with ICl in HCl 4-(3,5-diiodo-4-hydroxyphenacylamino)-3-iodobenzoic acid (XXV), m. 220-5°, was obtained. XIX (6.38 g.) in dioxane by warming with 2.74 g. XXII and 1.6 ml. pyridine gave 1-(4-benzoyloxyphenacyl)pyridinium bromide (XXVI), m. 240° (EtOH). Alternatively XXV was obtained by refluxing 4.66 g. β-bromo-3,5-diiodo-4-hydroxyacetophenone (prepd. from 3,5-diiodo-4-hydroxyacetophenone on bromination in CHCl3 under ultraviolet light) in dioxane, cooling, filtering, dissolving the ppt. in 10% Na2CO3 and repptg. with HCl. 5-Iodoisatin (2 g.) in 30% KOH was treated with 3-H2NC6H4Ac in EtOH and acidified with AcOH to give 2-(3-aminophenyl)6-iodoquinoline-4-carboxylic acid, m. 248-50° (EtOH), which on treatment in dil. HCl with ICl at 70° gave 2-(2,4,6-triiodo-3-aminophenyl)-6-iodoquinoline-4-carboxylic acid, m. 215° (decompn.).

IT 909884-05-5P, Sulfanilic acid, N-acetyl-, ester with N-(N-acetylsulfanilyl)tyrosine
RL: PREP (Preparation)
(preparation of)

RN 909884-05-5 CAPLUS

CN Sulfanilic acid, N-acetyl-, ester with N-(N-acetylsulfanilyl)tyrosine (7CI) (CA INDEX NAME)

Absolute stereochemistry.



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ACCESSION NUMBER: 1962:13172 CAPLUS
DOCUMENT NUMBER: 56:13172
ORIGINAL REFERENCE NO.: 56:2505h-i,2506b-i,2507a-i,2508a-e
TITLE: Amino acids and peptides. XXXV. Analogs of oxytocin modified in position 1 and 2 of the peptide chain: Protected intermediates
AUTHOR(S): Jost, K.; Rudinger, J.; Sorm, F.
CORPORATE SOURCE: Ceskoslov. Akad. Ved, Prague
SOURCE: Collection of Czechoslovak Chemical Communications (1960), 26, 2496-510
CODEN: CCCCAK; ISSN: 0010-0765
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. CA 55, 27107a.-N,O-Dimethyl-N-tosyl-L-tyrosine (2 g.), 10 g. PhOH, and 30 ml. 35% HBr in AcOH were heated in a pressure flask 105 min. at 65°, the solution was evaporated to dryness, the residue washed with 200 ml. Et2O, dissolved in 5% aqueous HBr, the solution washed 5 times with Et2O, brought to pH 7 with aqueous NH3, and cooled to 0° to give 0.54 g. N-methyl-L-tyrosine (I), [α]20D 19.4 ± 0.5° (c 3.5, 3.4 N HCl). If only 2 equivs. of PhOH were used, the product contained 22.6% Br. A reproducible separation of L-tyrosine, O-methyl-L-tyrosine, I, and I Me ester was obtained on a chromatoplate coated with silica gel with 3:1 PhOH-H2O as the solvent system. Esterification of 0.5 g. I with MeOH-HCl as usual gave 0.51 g. I Me ester-HCl (II), m. 145-7° (MeOH-Et2O). p-Fluorophenyl-L-alanine Et ester-HCl (III), m. 180-1° (EtOH-Et2O), and O-tosyl-L-tyrosine Me ester-HCl, m. 146-7° (MeOH-Et2O), were also prepared N-Tosyl-S-benzyl-L-cysteine (8 g.) in 25 ml. 2N NaOH and 15 ml. H2O was treated, with agitation, with 6 ml. Me2SO4 in 1 ml. portions and in 5 min. intervals, the pH being kept at 8-9 by addition of more 2N NaOH. The mixture was stirred 1 hr., extracted with EtOAc, the extract washed with 2N NaOH, H2O, 10% aqueous HCl, and H2O, dried, and evaporated to give 4.25 g. N-methyl-N-tosyl-S-benzyl-L-cysteine (IV) Me ester (IVa), m. 87-88° (MeOH or EtOAc-petr. ether or aqueous MeOH). IVa (2 g.), 25 ml. dioxane, 10 ml. MeOH, and 6 ml. 2N NaOH were kept 1 hr. at room temperature, the solution was diluted with H2O, acidified with concentrated aqueous HCl, extracted with EtOAc, the dried extract evaporated, the residue in C6H6 treated with 1.25 ml. freshly distilled dicyclohexylamine, the mixture diluted with petr. ether, cooled to 0°, the precipitate collected, and washed with petr. ether to give 2.56 g. IV dicyclohexylamine salt, m. 132-33° (C6H6-petr. ether). Keeping 0.5 g. IVa with 2 ml. anhydrous N2H4 10 days, collecting, and washing with H2O gave 0.3 g. IV hydrazide, m. 141-2° (EtOH). III (3.2 g.) in 12 ml. H2O and 50 ml. EtOAc was stirred and cooled to 0° while 4.3 g. K2CO3 in 15 ml. H2O was added, followed by 4.6 g. N-tosyl-S-benzyl-L-cysteinyl chloride in 10 ml. EtOAc. The mixture was stirred 1 hr. at room

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temp., the EtOAc layer sepd., washed with 5% aq. HCl, H2O, 5% aq. NaHCO3, and H2O, dried, and evapd. to give 6.37 g. N-tosyl-S-benzyl-L-cysteinyl-p-fluorophenyl-L-alanine Et ester, m. 85-86° (aq. EtOH), [α]23D -8.5 ± 0.1° (c 3.6, dioxane). Similarly were prepd. N-tosyl-S-benzyl-L-cysteinyl-O-benzyl-L-tyrosine Me ester (V), m. 130-1° (iso-PrOH-petr. ether), and N-tosyl-S-benzyl-L-cysteinyl-O-tosyl-L-tyrosine Me ester, m. 74-5° (Et2O-petr. ether). V (0.32 g.) in 10 ml. dioxane and 6 ml. 2N NaOH was stirred with 0.15 ml. Me2SO4 4 hrs. at room temp., the mixt. brought to pH 1 with aq. HCl, concd. in vacuo, the aq. supernatant decanted, and the residual oil kept over P2O5 in a desiccator to give 0.08 g. N-methyl-Ntosyl-S-benzyl-L-cysteinyl-O-benzyl-L-tyrosine Me ester monohydrate, m. 71-4° (iso-PrOH-petr. ether) (strongly dependent on the rate of heating). L-Tyrosine Et ester (7.2 g.) and 11.3 g. N-carbobenzoxy-S-benzyl-L-cysteine in 55 ml. MeCN were kept with 7.9 g. dicyclohexylcarbodiimide in 25 ml. MeCN 12 hrs. at room temp., the mixt. treated with 0.5 ml. AcOH, and after 30 min. the dicyclohexylurea removed by filtration. The filtrate was evapd., the residue dissolved in EtOAc, the soln. washed with 10% aq. HCl, H2O, 5% aq. NaHCO3, and H2O, dried, and evapd. to give 16.3 g. N-carbobenzoxy-S-benzyl-L-cysteinyl-L-tyrosine Et ester (VI), m. 104-5° (EtOAc-petr. ether or MeOH-N HCl or iso-PrOH-petr. ether), [α]20D 23 ± 2° (c 4.5, CHCl3). VI (1 g.) was kept with 6 ml. 30% HBr in AcOH 10 min. at room temp. and 5 min. at 60°, the mixt. poured into 150 ml. Et2O, chilled to -60°, the ppt. collected, washed with Et2O, and recrystd. from EtOH-Et2O to give 0.67 g. crude S-benzyl-L-cysteinyl-L-tyrosine Et ester-HBr (VII), m. 130-5° (in an other expt., m. 167-72° was observed), homogeneous in paper chromatography and paper electrophoresis; 3 addnl. crystns. from EtOH-Et2O, attended by large losses, raised the m.p. to 180-1°. The mixed anhydride prepd. from 0.11 g. N-carbobenzoxyglycine, 0.07 ml. N-ethylpiperidine, and 0.07 g. sec-BuOCOCl in 5 ml. CHCl3 at 0° was treated with 0.24 g. VII and 0.07 g. N-ethylpiperidine in 6 ml. CHCl3. After 1 hr. at room temp. the soln. was evapd. in vacuo, the residue taken up in EtOAc and H2O, the EtOAc layer washed with 10% aq. HCl, H2O, 5% aq. NaHCO3, and H2O, dried, and evapd. to give 0.22 g. N-carbobenzoxyglycyl-S-benzyl-L-cysteinyl-L-tyrosine Et ester, m. 98-101° (iso-PrOH-petr. ether). Similarly were prepd. N-tosylsarcosyl-S-benzyl-L-cysteinyl-L-tyrosine Et ester hemihydrate, m. 87-8° (iso-PrOH-petr. ether), and N-carbobenzoxy-L-leucylglycylglycyl-S-benzyl-L-cysteinyl-L-tyrosine Et ester hemihydrate, m. 105-8° (iso-PrOH-petr. ether).
N-Tosyl-S-benzyl-D-cysteinyl-L-tyrosine hydrazide (m. 193-4°) (3.64 g.), 20 ml. AcOH, 2.4 ml. 7.6N HCl, 1.6 ml. H2O, and 7.6 ml. Et2O were treated at -15° (with agitation) with 0.52 g. recrystd. NANO2 in 2 ml. H2O, the mixt. stirred 5 min. at -15°, dild. with 40 ml. Et2O, the soln. washed with a precooled (-10°) satd. NaHCO3 soln. in 16.8% aq. NaCl, briefly dried over Na2SO4 and added to 1.34 g. freshly distd. L-isoleucine Me ester in 5 ml. EtOAc. The mixt. was kept 24 hrs. at 0°, dild. with excess petr. ether, kept 2 days at 0°, the ppt. collected, and washed with petr. ether to give 4.04 g. N-tosyl-S-benzyl-D-cysteinyl-L-tyrosyl-L-isoleucine Me ester, m.

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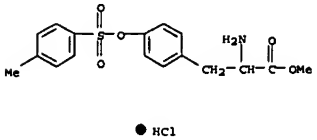
74-5° (Et2O-petr. ether), dihydrate, m. 154-5° (Et2O-petr. ether). N-Tosyl-S-benzyl-L-cysteinyl-O-methyl-L-tyrosyl-L-isoleucine Me ester, m. 155-6° (aq. MeOH), was prepd. similarly. The following hydrazides were prepd. by the action of N2H4 on the appropriate protected peptide esters: N-tosyl-S-benzyl-L-cysteinyl-L-leucine hydrazide (VIII), m. 195-6° (aq. MeOH); N-C tosylsarcosyl-S-benzyl-L-cysteinyl-L-tyrosinehydrazide, m. 233-4° (aq. EtOH); N-tosyl-S-benzyl-D-cysteinyl-L-tyrosyl-L-isoleucine hydrazide, m. 231-3°; N-tosyl-S-benzyl-L-cysteinyl-O-methyl-L-tyrosyl-L-isoleucine hydrazide, m. 228-30°; N-carbobenzoxyglycyl-S-benzyl-L-cysteinyl-L-tyrosine hydrazide, m. 212-13° (aq. MeOH); N-tosyl-S-benzyl-O-methyl-L-tyrosine hydrazide, m. 182-3°; Ntosyl-S-benzyl-L-cysteinyl-p-fluorophenyl-L-alanine hydrazide, m. 189-90°; N-methyl-N-tosyl-S-benzyl-L-cysteinyl-O-benzyl-L-tyrosine hydrazide monohydrate, m. 171-2°; and N-carbobenzoxy-L-leucylglycylglycyl-S-benzyl-L-cysteinyl-L-tyrosine hydrazide, m. 193-4°. II (0.23 g.) with 0.39 g. N-tosyl-S-benzyl-L-cysteinyl chloride and 0.3 g. K2CO3 as above gave an oil which was refluxed in MeOH with 0.5 ml. 92% N2H4 hydrate 3 hrs., the soln. dild. with H2O, cooled to 0°, and the ppt. collected to give 0.43 g. Ntosyl-S-benzyl-L-cysteinyl-N-methyl-L-tyrosine hydrazide, m. 69-71° (iso-PrOH-petr. ether) (strongly dependent on the rate of heating); in later work, material of m.p. 128131° was obtained. IV (1.96 g.) in 30 ml. MeOH was kept with 1 ml. 4N KOH 1 hr. at room temp., the soln. dild. with H2O, brought to pH 1 with aq. HCl, extd. with EtOAc, the EtOAc soln. extd. with 5% aq. NaHCO3, the aq. soln. acidified, extd. with EtOAc, the ext. dried, evapd. in vacuo, the residue dried azeotropically with C6H6, refluxed with 15 ml. SOCl2 10 min., and the soln. worked up as usual to give the chloride which was dissolved in CHCl3 and treated with 1.5 g. L-tyrosine Me ester-HCl and 1.6 ml. N-ethylpiperidine in 15 ml. MeCN. After 15 min. at room temp. the mixt. was evapd., and the residue worked up as usual to give an oily tosyldipeptide ester which was kept with 80% N2H4 hydrate in EtOH 3 days, the mixt. dild. with H2O, cooled to 0°, the ppt. collected, washed with H2O, extd. with Et2O, and the ext. evapd: to give 37% N-methyl-N-tosyl-S-benzyl-L-cysteinyl-L-tyrosine hydrazide, m. 903° (iso-PrOH-petr. ether).
L-Glutaminyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycine amide (1.3 g.) in 10 ml. HCONMe2 was treated with 0.71 g. N-carbobenzoxy-L-isoleucine (IX) p-nitrophenyl ester (X) in 6 ml. EtOAc, the mixt. kept 2 days at room temp., dild. with 75 ml. EtOAc, cooled to 0°, the ppt. collected, washed with EtOAc, 1% Na2CO3 aq., and H2O, dried, and crystd. to give 1.19 g. N-carbobenzoxy-L-isoleucyl-L-glutaminyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycine amide monohydrate (XI), m. 227-9° (aq. AcOH), [α]20D -46.6 ± 0.4° (c 0.58, HCONMe2). In earlier runs, a soln. of X prepd. from IX and p-O2NC6H4OH by the action of dicyclohexylcarbodiimide in tetrahydrofuran was directly used, after the removal of dicyclohexylurea. The amt. of active X was detd. by treating an aliquot of the soln. with cyclohexylamine: IX cyclohexylamide, m. 192-3°. XI (1.25 g.) in 3.5 ml. AcOH was treated with 14.5 ml. 35% HBr in AcOH 30 min. at 37°, the soln. dild. with Et2O, the ppt. washed 3 times with Et2O by decantation, dried in a desiccator, dissolved in 10 ml. H2O, the soln. filtered through Amberlite IRA-400 (OH cycle), the ninhydrin-pos. eluates dried from the frozen state, and the product (0.95 g.) repptd. from HCONMe2 soln. with EtOAc to give L-isoleucyl-L-glutaminyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycine amide (XII). 3.75M NANO2 (0.3 ml.) was added with agitation at -15° to 0.5 g. VIII in 7 ml. tetrahydrofuran and 0.5 ml. azeotropic aq. HCl, the mixt. stirred at -15° 8 min. more, dild. with 14 ml. EtOAc, the soln. washed at -15° with a 3% soln. of NaHCO3 in 16.8% aq. NaCl, dried over Na2SO4, and added to 0.77 g. XII in 28 ml. HCONMe2. The mixt. was kept 12 hrs. at 0°, evapd. in vacuo, the residue ground with dil. aq. HCl, collected, washed with H2O, dissolved in HCONMe2, and repptd. with H2O to give 1.08 g. N-tosyl-S-benzyl-L-cysteinyl-L-leucyl L-isoleucyl-L-glutaminyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycine amide monohydrate, m. 233-6°, [α]20D -27.8 ± 0.4 (c 0.482, CHCl3). Similarly were prepd. the following acyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycine amides (acyl, m.p., and [α]20D with c in CHCl3 given): N-tosyl-S-benzyl-L-cysteinyl-L-tyrosyl deriv. monohydrate, 241-3°, -35.8 ± 1.0°, 0.206; N-tosyl-S-benzyl-L-cysteinyl-O-methyl-L-tyrosyl deriv. monohydrate (XIII), 230-2°, -31.5 ± 1.0°, 0.197; N-tosyl-S-benzyl-L-cysteinyl-p-fluorophenyl-L-alanyl deriv. monohydrate, 231-6°, -39.3 ± 0.8°, 0.237; N-tosyl-S-benzyl-D-cysteinyl-L-tyrosyl deriv. monohydrate (XIV), 239-42°, -31.7 ± 0.4°, 0.530; N-tosyl-S-benzyl-L-cysteinyl-N-methyl-L-tyrosyl deriv. monohydrate, 127-30°, -39.3 ± 1.7°, 0.117; N-tosyl-N-methyl-S-benzyl-L-cysteinyl-L-tyrosyl, 193-6°, -36.6 ± 2.0°, 0.101; N-carbobenzoxyglycyl-S-benzyl-L-cysteinyl-L-tyrosyl deriv. dihydrate, 233-5°, -49.4 ± 2.4°, 0.085; N-tosylsarcosyl-S-benzyl-L-cysteinyl-L-tyrosyl deriv. tetrahydrate, 224-6°, -41.6 ± 1.0°, 0.214; and N-carbobenzoxy-L-leucylglycylglycyl-S-benzyl-L-cysteinyl-L-tyrosyl deriv. monohydrate, 239-41°, -38.7 ± 0.4°, 0.522. XIII and XIV were also prepd. from tosyltripeptide azide and hexapeptide amide. Samples of the above protected nona-, deca-, and dodecapeptides were reduced with Na in NH3, the products oxidized with air, and the solns. obtained assayed against a soln. of oxytocin prepd. in parallel. Some results of preliminary pharmacol. tests were briefly reported.

IT 94675-65-7P, Tyrosine, methyl ester, p-toluenesulfonate, hydrochloride 96582-66-0P, Tyrosine, N-[3-(benzylthio)-N-(p-tolylsulfonyl)-L-alanyl]-, methyl ester, p-toluenesulfonate, L-
RL: PREP (Preparation)
(preparation of)

RN 94675-65-7 CAPLUS
CN Tyrosine, methyl ester, p-toluenesulfonate, hydrochloride (7CI) (CA INDEX NAME)



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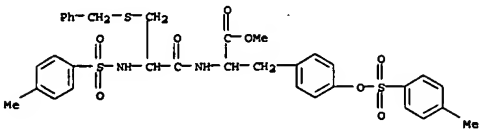
RN 96582-66-0 CAPLUS
CN Tyrosine, N-[3-(benzylthio)-N-(p-tolylsulfonyl)-L-alanyl]-, methyl ester, p-toluenesulfonate (7CI) (CA INDEX NAME)



L4 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:33963 CAPLUS
DOCUMENT NUMBER: 54:33963
ORIGINAL REFERENCE NO.: 54:6566g-i,6567a-i,6568a-e
TITLE: Di-o-phenylene pyrophosphite: a new reagent for peptide synthesis. II. Some peptide syntheses with the new reagent
AUTHOR(S): Crofts, P. C.; Markes, J. H. H.; Rydon, H. N.
CORPORATE SOURCE: Coll. Sci. Technol., Manchester, UK
SOURCE: Journal of the Chemical Society (1959) 3610-16
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 54:33963
AB cf. C.A. 53, 7080c. The use of di-o-phenylene pyrophosphite (I), as a reagent for the synthesis of peptides is described. The exptl. procedure is simple and the yields are good, and, although racemization occurs in certain circumstances, the new method is recommended for general use. Ester-interchange during the catalytic hydrogenolysis of peptide benzyl esters can be avoided by using Me3COH as solvent. The benzyl ester toluene-p-sulfonates were prepared by refluxing 0.1 mole of the amino-acid or peptide and 0.1 mole p-MeC6H4SO3H.H2O with 100-250 ml. PhCH2OH in 1-4 vols. of C6H6 in an apparatus fitted with a Dean and Stark tube to remove entrained H2O. Refluxing was continued for some hrs. after H2O ceased to be produced; C6H6 and some excess PhCH2OH were removed in vacuo at a maximum temperature 125°, and the residue was ground and slurried with Et2O. The insol. product was then recrystd. The following were prepared in this way: glycine benzyl ester toluene-p-sulfonate (II), m. 132° [MeOH-(iso-Pr)2O]; glycylglycine benzyl ester toluene-p-sulfonate (III), m. 153° (EtOH); L-leucine benzyl ester toluene-p-sulfonate (IV), m. 157° (C6H6-petr. ether), [α]23.5D 0.0° (c 2.00 in EtOH); DL-methionine benzyl ester toluene-p-sulfonate (V), m. 129-31° (AcOEt); DL-phenylalanine benzyl ester toluene-p-sulfonate (VI), m. 149° (H2O); and L-tyrosine benzyl ester toluene-p-sulfonate (VII), m. 175° (H2O), [α]23D -10.3° (c 1.00, 60% Me2CO). Unless otherwise stated, the following standard procedure was employed for the peptide syntheses. Equimol. amts. of carboxylic acid and amino-reactants, in anhydrous pyridine, were heated 30 min. with 10% excess I on a steam bath, cooled, poured into ice and H2O, next morning the product separated, filtered off, if solid washed with 1N NaHCO3, 1N HCl, and H2O, dried and recrystd.; if an oil it was dissolved in AcOEt, washed similarly, dried and recovered. In the "amide" procedure, the aminoreactant was heated 2 min. in pyridine on the steam-bath with I before addition of the carboxylic acid reagent. In the "anhydride" procedure the carboxylic reagent and I were similarly heated together 2 min. before addition of the amine reactant. N-Benzyloxycarbonylglycine (8.37 g.) (VIII), and 15.74 g. IV, coupled in 25 ml. pyridine by using 12.94 g. I, yielded 16.1 g. N-benzyloxycarbonylglycyl-L-leucine benzyl ester, an oil, which on repptn. from AcOEt with petr. ether gave 12.6 g. peptide benzyl ester, an oil,

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[α]19D -11.1° (c 2.39, AcOEt). The Me ester, prepd. similarly in 88% yield from L-leucine Me ester HCl salt, was an oil, [α]20.5D -9.0° (c 2.05, dioxane). Sapon. with 1N NaOH 45 min. followed by acidification afforded 31% N-benzyloxycarbonylglycyl-L-leucine, m. 102° (aq. EtOH), [α]20D -18.3° (c 1.39, 1N NaOH). N-Phthaloylglycine (6.15 g.) and 11.30 g. VII were coupled in 20 ml. pyridine by using 9.70 g. I; several recrystns. of the crude product gave 8.20 g. N-phthaloylglycyl-L-tyrosine benzyl ester, m. 189° (AcOEt-petr. ether), [α]19D 54.4° (c 1.43, AcOEt). Shaking 4.50 g. of this ester in 150 ml. EtOH and 30 ml. H2O in H with 5% Pd-C, gave 2.42 g. N-phthaloylglycyl-L-tyrosine, m. 257-8° [MeOH-(iso-Pr)2O], [α]21D 75.0° (c 1.00, 80% Me2CO). VIII (2.66 g.), and 4.73 g. S-benzyl-L-cysteine benzyl ester toluene-p-sulfonate, coupled in 10 ml. pyridine with 3.23 g. I, gave after recrystn. of the solid product 4.05 g. N-benzyloxycarbonyldiglycyl-S-benzyl-L-cysteine benzyl ester, m. 115.5-16.5° (AcOEt-petr. ether), [α]22.5D -35.0° (c 0.54, EtOH). N-Benzyloxycarbonyl-S-benzyl-L-cysteine (1.725 g.) and 1.615 g. III, coupled in 3.5 ml. pyridine by using 1.615 g. I, yielded 1.58 g. N-benzyloxycarbonyl-S-benzyl-L-cysteinylglycylglycine benzyl ester monohydrate, m. 135°, [α]18D -14.7° (c 1.01, AcOEt). The Et ester, prepd. similarly from glycylglycine Et ester HCl salt in 52% yield and recrystd. from AcOEt-petr. ether m. 111-13°, [α]18D -12.0° (c 3.21, EtOH). VIII (2.66 g.) and 3.37 g. II, coupled in 10 ml. pyridine by using 3.23 g. I, yielded 3.28 g. N-benzyloxycarbonyldiglycylglycine benzyl ester, m. 161° (EtOH). N-Benzyloxycarbonyl-L-leucine (7.95 g.) and 11.82 g. III, coupled in 21 ml. pyridine by using 9.70 g. I, yielded 9.7 g. N-benzyloxycarbonyl-L-leucylglycylglycine benzyl ester, m. 122-3° (AcOEt-petr. ether), [α]21D -11.7° (c 2.00, dioxane). This ester (5.30 g.), in 150 ml. tert-BuOH and 30 ml. H2O was shaken in H over 5% Pd-C, 10 ml. portions H2O being added from time to time to keep the peptide in soln. When absorption was complete, the mixt. was heated on the steam bath for a few min., filtered hot, when evapn. of the filtrate gave 1.47 g. L-leucylglycylglycine, [α]21D 57.2° (c 5.01, H2O). The crude tripeptide gave L-leucine and glycine when hydrolyzed 24 hrs. on a steam bath with const. boiling HCl. N-Benzyloxycarbonyl-DL-methionine (2.83 g.) and 3.94 g. III, coupled in 7 ml. pyridine by using 3.23 g. I, yielded 2.85 g. N-benzyloxycarbonyl-DL-methionylglycylglycine benzyl ester, m. 115.5-17.0° (EtOH). N-Benzyloxycarbonyl-L-tyrosine (0.75 g.) and 0.95 g. III, coupled in 2 ml. pyridine by using 0.81 g. I, yielded 0.31 g. N-benzyloxycarbonyl-L-tyrosylglycylglycine benzyl ester, m. 136° (AcOEt-petr. ether and EtOH), [α]18D -8.5° (c 1.40, Me2CO). N-Benzyloxycarbonylglycyl-L-leucine (3.23 g.) and 3.37 g. II, coupled in 7 ml. pyridine with 3.23 g. I, yielded 1.76 g. N-benzyloxycarbonylglycyl-L-leucylglycine benzyl ester, m. 127-8° (EtOH), [α]16.5D -15.4° (c 2.00, EtOH). This material hydrogenolyzed as usual in aq. tert-BuOH over Pd-C yielded glycyl-L-leucylglycine, [α]17.5D -19.3° (c 2.50, H2O), indicating 55% racemization. A similar coupling by the "amide" procedure gave 82% crude product with extensive racemization. N-Phthaloylglycyl-L-tyrosine (0.368 g.) and 0.377 g. II, coupled in 1.5 ml. pyridine with 0.300 g. I, yielded 0.07 g. N-phthaloylglycyl-L-tyrosylglycine benzyl ester, m. 167-9°, [α]20D 14.6° (c 0.65, 2-ethoxyethanol). Acid hydrolysis gave

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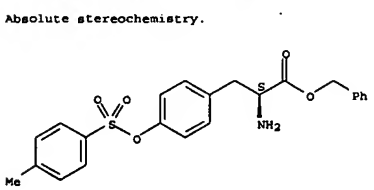
a product from which 10% DL-tyrosine was isolated. Neither the yield nor the quality of the product was improved by using the "amide" coupling procedure. VIII (7.98 g.) and 11.80 g. IV, coupled in 21 ml. pyridine with 9.70 g. I, yielded a yellow oil from AcOEt, which crystd. on trituration with AcOEt-petr. ether, and was suspended in 250 ml. boiling Et2O and pptd. with petr. ether. The solid gave 9.86 g. pure N-benzyloxycarbonyldiglycyl-L-leucine benzyl ester, m. 93-4°, [α]23.5D 0.0 (c 2.00, CHCl3). This ester (9.10 g.), in 170 ml. tert-BuOH and 30 ml. H2O shaken 34 hrs. in H over 5% Pd-C. yielded 4.15 g. diglycyl-L-leucine monohydrate, m. 217° (decompn.) (H2O), [α]19D -29.9° (c 2.00, H2O). VIII (5.32 g.) and 8.23 g. V, coupled in 10 ml. pyridine with 7.35 g. I, yielded a gummy product isolated from AcOEt which crystd. on addn. of petr. ether to a concd. soln. in AcOEt. Recrystn. from AcOEt-petr. ether gave 3.90 g. N-benzyloxycarbonyldiglycyl-DL-methionine benzyl ester, m. 92-4°. VIII (2.66 g.) and 4.27 g. VI, coupled in 10 ml. pyridine with 3.23 g. I, yielded 3.52 g. N-benzyloxycarbonyldiglycyl-DL-phenylalanine benzyl ester, m. 113-13.5° (aq. EtOH). N-Benzyloxycarbonylglycylglycine (5.32 g.) and 8.87 g. VII, coupled in 13 ml. pyridine with 7.06 g. I, yielded 4.71 g. N-benzyloxycarbonyldiglycyl-L-tyrosine benzyl ester, m. 161° (aq. MeOH), [α]19D 12.8° (c 2.00, dioxane). N-Benzyloxycarbonylglycylglycine (2.66 g.) and 3.95 g. III, coupled in 10 ml. pyridine with 3.23 g. I, yielded 3.29 g. N-benzyloxycarbonyltriglycylglycine benzyl ester, m. 199-200° (aq. pyridine). N-Benzyloxycarbinolglycyl-L-phenylalanine (1.42 g.), 0.41 g. redistd. glycine Et ester, and 1.29 g. I in 5 ml. di-Et phosphite heated 30 min. on a steam bath, the mixt. cooled, treated with 20 ml. H2O, the pptd. oil dissolved in AcOEt and washed with 1N HCl, 1N Na-HCO3, and H2O, dried and recovered, gave by addn. of H2O to a concd. soln. in EtOH the extensively racemized N-benzyloxycarbonylglycyl-L-phenylalanylglycine Et ester, m. 123-4°, [α]18.5D -1.6° (c 2.00, EtOH).
IT 102559-49-9P, Tyrosine, benzyl ester, p-toluenesulfonate
RL: PREP (Preparation)
(preparation of)
RN 102559-49-9 CAPLUS
CN L-Tyrosine, phenylmethyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

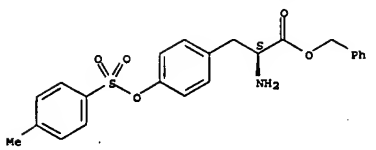
Absolute stereochemistry.



L4 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1959:28704 CAPLUS
DOCUMENT NUMBER: 53:28704
ORIGINAL REFERENCE NO.: 53:5148g-i,5149a
TITLE: Synthesis of amino acid benzyl ester p-toluenesulfonates
AUTHOR(S): Izumiya, Nobuo; Makisumi, Satoru
CORPORATE SOURCE: Kyushu Univ., Fukuoka
SOURCE: Nippon Kagaku Zasshi (1957), 78, 662-4
CODEN: NPKZAZ; ISSN: 0369-5387
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The following benzyl ester p-toluenesulfonates of amino acids were prepared
by heating 0.1 mol amino acid, 0.1 mol p-MeC6H4SO3H.H2O (I), and 60-80 cc.
PhCH2OH (II) at 110-20° until a clear solution was obtained, repeatedly removing II in vacuo, and crystallizing from EtOH-Et2O (amino acid,
m.p., [α]13D of 2% solution given): glycine, 132°, -; β-alanine, 138-9°, -; L-alanine, 114°, -6.8° (H2O); D-alanine, 113-14°, -6.9° (H2O); Me2C(NH2)CO2H, 154°, -; L-EtCH(NH2)CO2H, 117°, -6.3° (EtOH); L-valine, 157-9°, -3.5° (EtOH); L-leucine, 154-5°, 0.5° (EtOH); L-norleucine, 127°, -9.0° (EtOH); L-PhCH2CH(NH2)CO2H, 165°, 7.2° (HCONMe2); L-tyrosine, 174-5°, -5.6° (HCONMe2); L-asparagic acid, 151-2°, -4.0° (HCONMe2); L-hydroxyproline-H2O, 107-9°, -21.8° (H2O). Glutamic acid on similar treatment gave a solid (III), m. 120-30°, which could be purified by dissolving 37.6 g. III in 1.2 l. H2O and about 150 cc. EtOH and cooling. Dibenzyl glutamate p-tosylate,
needles, m. 142°, [α]13D 8.2° (HCONMe2). Lysine (IV), arginine (V), or histidine (VI).HCl was treated with 0.24 mol I giving IV benzyl ester di-p-tosylate, m. 147-9°, [α]13D -2.8° (H2O). V, L-proline, nitro-L-arginine, and DL-threonine failed to give crystalline product, VI gave a very hygroscopic one, L-tryptophan gave a colored product, and L-methionine gave crystals too small to filter off. To confirm that racemization did not occur in the esterification, L-MeCH(NH2)CO2CH2Ph.MeC6H4SO3H-p was converted to HCl salt, m. 139-40°, [α]15D -11.2° (2%, N HCl), by neutralizing in CHCl3 with Et3N and introducing HCl.
IT 102559-49-9P, Tyrosine, benzyl ester, p-toluenesulfonate
RL: PREP (Preparation)
(preparation of)
RN 102559-49-9 CAPLUS
CN L-Tyrosine, phenylmethyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

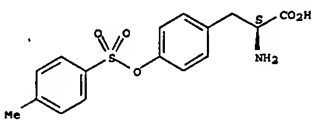
Absolute stereochemistry.

L4 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1959:12910 CAPLUS
DOCUMENT NUMBER: 53:12910
ORIGINAL REFERENCE NO.: 53:2453i,2454a
TITLE: Effect of tyrosine antimetabolites on the radioiodine uptake of the thyroid gland
AUTHOR(S): Sos, J.; Kertai, P.; Nagy, J.; Csuzi, S.
CORPORATE SOURCE: Univ. Med., Budapest
SOURCE: Acta Physiologica Academiae Scientiarum Hungaricae (1958), 14, 57-9
CODEN: APACAB; ISSN: 0001-6756
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Administration of p-hydroxyphenylglycine failed significantly to influence
I uptake by the thyroid. Tosyltyrosine definitely inhibited both thyroglobulin synthesis and I uptake.
IT 13504-89-7, Tyrosine, p-toluenesulfonate
(effect on I uptake by thyroid gland)
RN 13504-89-7 CAPLUS
CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1958:45209 CAPLUS
DOCUMENT NUMBER: 52:45209
ORIGINAL REFERENCE NO.: 52:8048h-i,8049a-i,8050a-i
TITLE: Arginine peptides. I. Intermediates in the synthesis of N-terminal and C-terminal arginine peptides
AUTHOR(S): Zervas, Leonidas; Winitz, Milton; Greenstein, Jesse P.
CORPORATE SOURCE: Natl. Insts. of Health, Bethesda, MD
SOURCE: Journal of Organic Chemistry (1957), 22, 1515-21
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 52:45209
AB cf. C.A. 51, 5152d. Nα tricarbobenzyloxy-L-arginine (I) prepared in strongly alkaline medium by carbobenzyloxylation of L-arginine (II), a mixture
of at least 2 isomeric forms, boiled in alc. gave, Nα,Nω-dicarbobenzyloxy-L-arginine (III) and a single pure isomer (IIIa) of I, acidified to give pure tricarbobenzyloxy-L-arginine (IV). The utility of IV in the preparation of N-terminal arginine peptides was demonstrated and IV
was transformed through III into N-carbobenzyloxy-L-arginine and its PhCH2
and Me esters, of potential value in the synthesis of C-terminal arginine peptides. II.HCl (42.2 g.) in 400 ml. N NaOH at 2-5° treated in 30 min. alternately with 5 portions 100 ml. 2N NaOH and 27.2 ml. freshly prepared PhCH2O2CCl with vigorous shaking and cooling (ice-bath) and the mixture stirred 30 min., the cold mixture filtered and the precipitate washed with
200 ml. cold 5% Na2CO3, the wet precipitate taken up in 1 l. cold alc.-free CHCl3
and the CHCl3 layer washed with 100 ml. cold 5% Na2CO3, dried (anhydrous Na2SO4) and concentrated at 25°/14 mm., the residue taken up in 1 l. dry Et2O and refrigerated 12 hrs., the product washed with dry Et2O, and dried
in vacuo over P2O5 gave 78-85 g. I. I (12 g.) in 100 ml. absolute alc. boiled
several min. and the hot solution filtered, the filtrate stored several hrs.
at 4° and filtered, the residue washed with cold alc. and Et2O, and recrystd. from hot absolute alc. gave 5.8 g. IIIa. The combined filtrate and
washings concentrated in vacuo and the residue taken up in hot MeOH gave 3.2 g.
III, m. 150°, [α]25D -10.0° (1%, C5H5N). II.HCl (42.2 g.) carbobenzyloxylated as above and the mixture filtered, the precipitate washed
with 100 ml. cold 5% Na2CO3 and taken up in 1 l. alc.-free CHCl3, the CHCl3 layer washed successively twice with 100 ml. 5% Na2CO3, twice with 100 ml. 2N H2SO4, and several times with H2O at 1-5°, the dried (Na2SO4) CHCl3 fraction concentrated at 35-40°/14 mm. and the residue taken up in alc., the solution evaporated in vacuo and the CHCl3-free residue
boiled 2 min. with 27 g. NaOAc.3H2O in 200-20 ml. hot alc. with stirring, the solution kept 12-20 hrs. at 20° and filtered, the precipitate washed with
30 ml. absolute alc. and taken up in 100 ml. boiling EtOAc, the filtered solution
chilled to 4° and filtered, the solid residue washed with 20 ml.

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cold EtOAc and the moist solid taken up in hot abs. alc., the soln. kept 24 hrs. at 4° and filtered, the ppt. washed with a little cold abs. alc., and then with dry Et2O gave 21-4 g. extremely pure Ia. EtOAc (100 ml.) contg. 2.5 g. Ia vigorously shaken with 25 ml. 2% H2SO4 and the EtOAc layer washed with 25 ml. 2% H2SO4, and 3 times with H2O, the dried soln. concd. in vacuo, and the cryst. residue triturated with petr. ether gave 1.9 g. material, twice recrystd. (EtOAc) to give IV, m. 138-9°, [α]25D 15.5° (1%, alc. free CHCl3). I (60 g.) added to 8 g. NaOH in 200 ml. MeOH with cooling (ice bath) and the mixt. kept 1 hr. at 20°, the soln. concd. to 100 ml. in vacuo and dild. with 500 ml. H2O and 20 ml. AcOH, the mixt. decanted and the gummy residue washed with H2O, taken up in hot MeOH and the soln. kept several hrs. at 20° and 4°, the product (38-40 g., m. 148°) taken up in dil. K2CO3 and the soln. acidified, filtered, and the gummy product crystd. from hot MeOH yielded III. III (22.1 g.) in 50 ml. N NaOH at 2-3° treated alternately in 10 min. with 3 portions of 2.83 ml. PhCH2O2CCl and 8.33 ml. 2N NaOH with vigorous shaking and cooling (ice-bath) and the mixt. stirred 30 min., filtered and the ppt. taken up in cold alc.-free CHCl3, the CHCl3 layer washed with 10 ml. 5% Na2CO3 (all operations below 4°) and the dried soln. evapd. at 20-5° in vacuo, the oily residue taken up in Et2O, and the soln. kept 12 hrs. at 4° gave 20 g. Ia. IV (2.9 g.) in 20 ml. purified SOCl2 kept 5 hrs. at room temp. and dild. with petr. ether, the sirupy product washed with petr. ether and taken up in 20 ml. Me2CO, the soln. treated with 0.5 ml. concd. HCl and stored 6 hrs. at room temp., concd. in vacuo at 40° and the residue taken up in H2O, the soln. filtered and made faintly alk. with KHCO3, filtered, and the product crystd. from MeOH gave 50% Nα,Nα-dicarbobenzyloxy-L-arginine (V), m. 160°. III (4.4 g.) in 30 ml. pure SOCl2 kept 1 hr. at 20° and concd. in vacuo at 40-5°, the residual sirupy Nα-carbobenzyloxy-L-arginine N-carboxyanhydride HCl salt washed free from PhCH2Cl with petr. ether and taken up in 50 ml. 10% AcOH, the soln. kept 4 hrs. at 20° and concd. in vacuo, the residue dissolved in 50 ml. H2O and the filtered soln. adjusted to pH 9 with concd. NH4OH kept 24 hrs. at room temp. in an open vessel, filtered and the ppt. washed with cold H2O, the product (2.6 g.) recrystd. from boiling alc. dild. dropwise with H2O, and the soln. treated with alc. stored at 4° gave Nα-carbobenzyloxy-L-arginine (VI), m. 190°, [α]25D 9.5° (6-12%, 1 equiv. dil. HCl). III (4.4 g.) in 30 ml. dry CHCl3 and 2.1 g. PCl5 shaken several min. at 0° and the soln. stored 1 hr. at room-temp., concd. in vacuo at 40-5° and the residue washed repeatedly with petr. ether, treated with 50 ml. 10% AcOH and the soln. stored 4 hrs. at 20°, washed twice with EtOAc and concd. in vacuo 40-5°, the oily residue taken up in 50 ml. H2O, and treated as above with aq. NH4OH yielded 65% VI. NaHCO3 (63 g.) in 250 ml. H2O stirred vigorously with 42.2 g. II HCl salt and the mixt. treated 5 times in 30 min. with 7.48 g. PhCH2O2CCl, the stirring continued 1 hr. and the mixt. adjusted to pH 8.5 with concd. NH4OH, stored 2 hrs. at 4° and filtered, the ppt. washed with cold H2O, and recrystd. from boiling H2O contg. a few drops NH4OH yielded 58.6 g. Nα-carbobenzyloxy-L-arginine (VII), m. 175°. III (4.4 g.) in 30 ml. pure SOCl2 kept 1 hr. at 20° and treated with petr. ether, the sirupy N-carboxyanhydride washed repeatedly with petr. ether and taken up in 30 ml. abs. MeOH contg. about 0.7 g. HCl, the mixt. kept

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hrs. at room temp. and evapd. in vacuo at 30-5°, MeOH added and the evapn. repeated, the sirup taken up in 7-8 ml. MeOH and treated with 60 ml. AcEt, the mixt. kept 24 hrs. at room temp. in an open vessel, filtered, and the ppt. washed with AcEt and Et2O gave 3.3 g. VI Me ester-2HCl.H2O (VIa), m. 110° (decompn.). III (4.4 g.) in 30 ml. pure SOCl2 kept 1 hr. at 20° and treated with petr. ether, the sirup washed with petr. ether and taken up in 20 ml. PhCH2OH contg. approx. 0.7 g. HCl, the mixt. stored 3 hrs. at 20° and dild. with dry Et2O, the pptd. sirup taken up in a small amt. of H2O treated with excess anhyd. K2CO3 and the product extd. with EtOAc, the ext. concd. in vacuo, and treated with petr. ether gave prismatic material, recrystd. (EtOAc) to give 82% VI benzyl ester, m. 121°. The ester (2 g.) kept 2 hrs. at 20° in 20 ml. dry CHCl3 with 2 ml. dry C5H5N and 0.6 ml. Ac2O and the mixt. washed thoroughly with 10% AcOH and aq. KHCO3, evapd., and the residue triturated with cold H2O gave 70% Nα-acetyl-N-carbobenzyloxy-L-arginine benzyl ester, m. 82° (EtOAc), transformed by hydrogenolysis in the presence of Pd catalyst to a nearly quant. yield of Nα-acetyl-L-arginine monohydrate, m. 270°, [α]D 7.8° (H2O). Glycine (18.8 g.), 48.5 g. p-MeC6H4SO3H.H2O, and 100 ml. PhCH2OH in 50 ml. C6H6 distd. azeotropically 2-5 hrs. with the aid of a Dean and Stark distg. receiver and the cooled H2O-free mixt. dild. with 250 ml. C6H6 and 400 ml. dry Et2O, the mixt. kept 2 hrs. at 4° and filtered, the product washed with dry Et2O, and recrystd. (MeOH-Et2O) yielded 84% salt. Similarly were prepd. a series of amino acid benzyl ester p-toluenesulfonates [amino acid, m.p. (cor.), and [α]25D (1-2%, MeOH) given]: D-alloisoleucine, 162-4°, -0.2°; L-aspartic acid, 158-60°, 1.0°; L-S-benzylcysteine, 162-3°, -20.9°; L-leucine, 158.5-60°, -1.7°; L-phenylalanine, 170.5-1.5, -7.2°; L-tyrosine, 179-80.5, -12.2°; L-Valine, 158-60, 1.2°. The over-all yields, in most instances, ranged from 80-90%. IV (2.85 g.) and 0.7 ml. anhyd. NEt3 in 15 ml. dry CHCl3 treated 15 min. at 0° with 0.47 ml. ClCO2Et and the mixt. kept 1 hr. at room temp. with 2.0 g. VI benzyl ester, the CHCl3 soln. washed with dil. AcOH and H2O, the dried ext. (anhyd. Na2SO4) evapd. in vacuo and freed from CHCl3 by evapn. from MeOH, the residue taken up in hot MeOH and treated with 0.3 ml. NEt3 (to prevent contamination with an unreacted tricarbobenzyloxy-L-arginine), the soln. cooled 12 hrs. at 4°, and the product washed with cold MeOH and Et2O gave 3.5 g. tricarbobenzyloxy-L-arginyl-N-carbobenzyloxy-L-arginine benzyl ester, m. 147-8° (MeOH). Similar condensation of 2.85 g. IV and 1.8 g. VIa gave 2.3 g. product, m. 128°, crystd. (EtOAc) to give the corresponding Me ester, m. 135°. In the same way, IV was condensed with VII in CHCl3 and the condensation product isolated in comparable manner, with the exception that the cryst. residue obtained on evapn. was first triturated with cold MeOH contg. NEt3, then filtered and recrystd. twice from EtOAc to yield 75% tricarbobenzyloxy-L-arginyl-L-glutamic acid benzyl ester, m. 120-1°, hydrogenolyzed in 95% AcOH in the presence of Pd-C and the mixt. filtered, the catalyst washed with MeOH and H2O and the combined filtrate and washings evapd. in vacuo, the residue taken up in hot EtOH and the soln. cooled and filtered, and the cryst. product recrystd. from H2O to give 90% L-arginyl-L-glutamic

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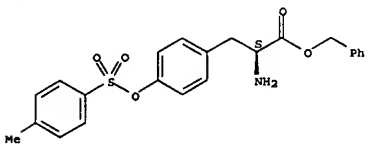
acid tetrahydrate, m. 210-14°, [α]24D 21.4° (1%, H2O), converted to anhydrous material on drying 2 hrs. in vacuo at 78°. The dipeptide hydrolyzed with 5N HCl and freed from excess acid in vacuo, the hydrolyzate taken up in H2O and spotted together with the dipeptide and amino acid reference standards on Whatman No. 1 paper, previously briefly exposed to NH3, the chromatograms developed with 3:3:14 HCO2H-H2O-Me3COH, 20:5:1 MeOH-H2O-C5H5N, 70% alc., or 88% PhOH with 10% NaOAc, and visualized with ninhydrin showed pos. spots for the dipeptide, Rf0.26, 0.28, 0.29, 0.53. The hydrolyzate revealed only 2 spots corresponding to glutamic acid and arginine, resp.

IT 102559-49-9P, Tyrosine, benzyl ester, p-toluenesulfonate
RL: PREP (Preparation)
(preparation of)

RN 102559-49-9 CAPLUS

CN L-Tyrosine, phenylmethyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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ACCESSION NUMBER: 1958:1658 CAPLUS
DOCUMENT NUMBER: 52:1658
ORIGINAL REFERENCE NO.: 52:262a-i,263a-f
TITLE: Synthetic studies on arginine-vasopressin: condensation of S-benzyl-N-carbobenzoxy-L-cysteinyl-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparagine and its O-tosyl derivative with S-benzyl-L-cysteinyl-L-prolyl-L-arginylglycinamide
AUTHOR(S): Katsoyannis, Panayotis G.; Gish, Duane T.; du Vigneaud, Vincent
CORPORATE SOURCE: Cornell Univ. Med. Coll., New York, NY
SOURCE: Journal of the American Chemical Society (1957), 79, 4516-20
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB S-Benzyl-L-cysteinyl-L-prolyl-L-arginylglycinamide-2HBr (I.2HBr) in about 4 parts HCONMe2 treated with about 10% excess Et3N with stirring, the mixture treated with CHCl3 (dropwise at first) and filtered, the residue washed with CHCl3 and dissolved in HCONMe2, the solution treated with 2-3 drops Et3N, diluted with CHCl3, and filtered, and the precipitate washed and dried in vacuo over P2O5 and NaOH yielded nearly 100% I.HBr.

S-Benzyl-N-carbobenzoxy-L-cysteinyl-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparagine (114 mg.), 75 mg. I.HBr, 0.09 g. [(EtO)2P]2O (II), and 0.45 cc. (EtO)2P(O)H (III) heated 50 min. at about 95°, the mixture cooled, diluted with Et2O, and filtered, the filter residue washed with Et2O, dried over P2O5 in vacuo, and treated with Na in liquid NH3, the NH3 evaporated, the residue dissolved in 200 cc. 0.1% AcOH, the solution adjusted to pH 6.7 with NH4OH, aerated 1 hr. with a slow stream of air, several similar solns. from a number of runs combined (total activity 66,000 pressor units; a value of 0.47 unit/mg. was assigned to the U.S. Pharmacopeia posterior pituitary standard powder; the activity in pressor units is given throughout this abstract in parentheses), concentrated in a rotary evaporator at 25°, and lyophilized, the residual mixture (about 4 g.) (58,000 units) subjected to a 690-transfer countercurrent distribution with EtMeCHOH-0.06M p-MeC6H4SO3H, the organic phase extracted with H2O, the combined aqueous extract and phase passed through Amberlite IR-45 (acetate form), and the effluent (45,000 units) concentrated and lyophilized gave 520 mg. powder; a 490-mg. sample in 3 cc. pyridine-AcOH buffer of pH 4.0 (24 cc. pyridine and 91 cc. AcOH diluted to 4 l. with H2O) subjected to electrophoresis on cellulose during 40 hrs. at 5° with a potential gradient of 9 v./cm., and the solns. from the 3 segments which exhibited the highest activity lyophilized yielded about 70 mg. powder (175 units/mg.). A sample in H2O assayed for pressor, antidiuretic, and avian vasodepressor activities showed a ratio of 1:1:0.15 (the ratio for natural arginine-vasopressin). The product chromatographed on Amberlite IRC-50 (XE-64) with 0.2M Na phosphate buffer of pH 6.95 gave only a single peak. The synthetic product and natural arginine-vasopressin (0.1 cc. solution each containing about 0.85 mg./cc.) subjected to paper electrophoresis side by side

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on Whatman No. 1 paper during 18 hrs. at 5° with a potential gradient of 9 v./cm. gave identical spots. The synthetic material hydrolyzed and chromatographed on starch gave the following fragments (molar ratios given): phenylalanine 1.2, tyrosine 1.2, proline 0.8, glutamic acid 1.3, aspartic acid 0.85, glycine 1.0, NH3 3.7, arginine 1.1, cystine 0.85, unknown 0.5. L-Tyrosine (18 g.) in 200 cc. N NaOH treated with 12.5 g. CuSO4.5H2O in 50 cc. H2O, stirred until dissolved, treated with 19 g. p-MeC6H4SO2Cl in 40 cc. Et2O, shaken 3.5 hrs., and filtered, the residual Cu complex washed with H2O, dissolved in 200 cc. concd. HCl, cooled several hrs., and filtered, the pptd. cryst. HCl salt dissolved in 1 l. H2O, the soln. adjusted to pH 6 with NH4OH and cooled, and the ppt. filtered, washed with H2O, dried (15 g.), and recrystd. from 1.5 l. boiling H2O gave 12.5 g. O-tosyl-L-tyrosine (IV), m. 215-17° (all m.ps. are cor.), [α]22D 9.0° (c 3.0, N HCl). IV (3.35 g.), 10 cc. N NaOH, 15 cc. N Na2CO3, and 80 cc. N NaHCO3 warmed a few min., cooled to 0°, treated during 1 hr. with 2 g. ClCO2CH2Ph in portions with stirring and cooling, the mixt. stirred 0.5 hr., acidified with HCl, stirred 15 min., and filtered, and the ppt. washed with H2O, dried, and repptd. from EtOAc with hexane gave 3.8 g. N-PhCH2O2C deriv. (V) of IV, m. 124-6°, [α]25D -27° (c 1, HCONMe2). V (0.7 g.) in 15 cc. AcOH satd. with HBr, kept 1 hr. at 25° with occasional stirring, evapd. in vacuo, mixed with 50 cc. H2O, adjusted to pH 6.0 with NH4OH, and filtered yielded IV. V (1.88 g.) and 0.4 g. Et3N in 12 cc. tetrahydrofuran treated at -10° with stirring with 0.55 g. iso-BuO2CCl, and after 10 min. with 1.7 g. L-phenyl-L-glutaminyl-L-asparagine and 0.43 g. Et3N in 9 cc. H2O, the mixt. warmed during 25 min. to room temp. and dild. with Et2O, the ppt. filtered off, washed with Et2O, suspended in 100 cc. H2O, acidified with HCl, and filtered, and the residue washed with H2O, dried, and triturated with EtOAc yielded 2.7 g. O-tosyl-N-carbobenzyloxy-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparagine (VI), m. 218-20° (50% AcOH), [α]25D -16.6° (c 1, HCONMe2). VI (2.55 g.) in 50 cc. 2N HBr in AcOH kept 1 hr. at 25°, dild. with Et2O, and filtered, the residue washed with Et2O, repptd. twice from MeOH with Et2O (1.92 g.) dissolved in 5 cc. H2O and 4.8 cc. N NaOH, cooled, added to the anhydride from 7.6 g. S-benzyl-N-carbobenzyloxy-L-cysteine and 0.32 g. iso-BuO2CCl with 0.24 g. Et3N in 12 cc. tetrahydrofuran, dild. with Et2O, and filtered, the residue suspended in 200 cc. H2O, acidified with HCl, and filtered, and the residue washed with H2O, dried, and triturated with EtOAc yielded 1.92 g. S-benzyl-N-carbobenzyloxy-L-cysteinyl-O-tosyl-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparagine (VII), m. 217-19° (pptd. from 70% AcOH), [α]25D -33.5° (c 1, HCONMe2). S-Benzyl-N-carbobenzyloxy-L-cysteinyl-L-proline (2.92 g.), 1.86 g. L-arginylglycinamide-HBr, 3.10 g. II, and 10 cc. III heated 0.5 hr. at 100°, cooled, and dild. with EtOAc, the ppt. filtered off, washed with EtOAc, and dried over P2O5 and NaOH, and the crude product subjected to a 120-transfer countercurrent distribution with EtMeCHOH-1% AcOH yielded 3.0 g. S-benzyl-N-carbobenzyloxy-L-cysteinyl-L-prolyl-L-arginylglycinamide-HBr (VIII), hygroscopic amorphous powder. VIII (2.87 g.) treated with 0.47 g. Na in 300 cc. liquid NH3, the blue color discharged with NH4Cl, the mixt. treated with 0.5 cc. PhCH2Cl, stirred 0.5 hr., treated with 1.09 g. NH4Cl,

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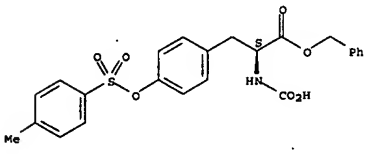

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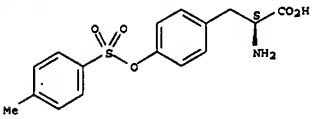
and evapd., the residue extd. with 30 cc. glacial AcOH in 3 portions, the combined exts. dild. with 400 cc. Et2O, the ppt. repptd. from 70 cc. AcOH with Et2O, and the amorphous ppt. dried in vacuo over P2O5 and NaOH and subjected to a 520-transfer countercurrent distribution with EtMeCHOH-1% AcOH gave 1.9 g. mixed HCl and HBr salts of S-benzyl-L-cysteinyl-L-prolyl-L-arginylglycinamide (IX), amorphous hygroscopic powder. VII (1.05 g.), 0.56 g. IX, 4 cc. III, and 0.56 g. II condensed in the usual manner, the mixt. dild. with H2O and filtered, the residue triturated with H2O, dried, treated with Na in liquid NH3, and oxidized in the usual manner gave an active soln. (22,000 units); the combined solns. from a no. of runs (57,000 units) concd. and lyophilized, the residual mixt. (about 6 g.) extd. with 50 cc. glacial AcOH, and the ext. filtered, dild. with 200 cc. abs. Et2O, and filtered yielded 1.95 g. polypeptide (21 units/mg.), which subjected to a 1100-transfer countercurrent distribution with EtMeCHOH-1% AcOH gave 400 mg. product (about 70 units/mg.); a portion (195 mg.) subjected to electrophoresis on a cellulose block with a pyridine-acetate buffer of pH 4 gave 63 mg. product (150 units/mg.); this material subjected to a 2000-transfer countercurrent distribution with EtMeCHOH-1% AcOH yielded 23 mg. product (220 units/mg.).

IT 13504-89-7P, Tyrosine, p-toluenesulfonate 121445-83-8P, Tyrosine, N-carboxy-, benzyl ester, p-toluenesulfonate
RL: PREP (Preparation)
(preparation of)

RN 13504-89-7 CAPLUS

CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 121445-83-8 CAPLUS

CN L-Tyrosine, N-carboxy-, 1-benzyl ester, p-toluenesulfonate (6CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1954:24942 CAPLUS
DOCUMENT NUMBER: 48:24942
ORIGINAL REFERENCE NO.: 48:4478h-i,4479a-i,4480a-i,4481a
TITLE: Synthesis of thyroxine and related substances. XII. Preparation of simple analogs of thyroxine
AUTHOR(S): Barnes, J. H.; Elks, J.; Stephens, F. F.; Waller, G. J.
CORPORATE SOURCE: Glaxo Labs., Ltd., Greenford, UK
SOURCE: Journal of the Chemical Society (1953) 764-77
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB cf. C.A. 47, 1127f. Ethers (ROR') related to thyroxine were prepared by condensation of substituted phenols with aryl or alkyl halides or p-toluenesulfonyl esters, or by reduction of the corresponding nitro compds., diazotization of the amines, and reaction with NaI (cf. C.A. 46, 8055h; 47, 1126g). They were tested for antithyroid activity in mice (cf. Sheahan, Wilkinson, and Maclagan, C.A. 45, 5316c). In the following table, where R or R' contains a substituted diiodophenyl residue, it is given as m,n,o-XD, where D is the diiodophenyl residue, X is the substituent, and m, n, and o are the positions of the substituent and the 2 iodine atoms, resp. Other intermediates include 4,6,2-I2MeC6H2OH, m. 65-6° (acetate, m. 72-4°), and 4,6,2-I2PrC6H2OH, m. 51-2° (acetate, m. 72-4°), obtained by iodination of the R, R', M.p., °C., [α]tD, Antithyroid activity; HO2CCH2, 4,2,6-MeD, 167, +; ", 4,2,6-Me3CD, 183-4; ", 2,4,6-MeD, 205-6, ++; EtO2CCH2, ", 72-3, ++; H2NCOCH2, ", 162; H2NNHCOCH2, ", 141, ++; EtO2CCH2, 2,4,6-PrD, 63-5, ++; ", 2,4,6-ID, +++; BuO2CCH2, ", 80-2, ++; H2NNHCOCH2 , ", 192 (211)°, -; HO2CCH2, 4,2,6-HO2CD, +; PhCH2, 4,2,6-DL-EtO2CCH(NHAc)CH2D, 126-9, ; ", 4,2,6-DL-HO2CCH(NHAc)CH2D, 78-88 (176-9)°, +++; ", 4,2,6-HO2CCH(NH2)CH2D, 208-9; ", 4,2,6-L-Et2OCCH(NHAc)CH2D, 152-4, 5420; ", 4,2,6-L-HO2CCH(NHAc)CH2D, 65-85(decomposition), 7020, +++; Me, 4,2,6-DL-EtO2CCH(NHAc)CH2D, 127-9, ; ", 4,2,6-DL-HO2CCH(NHAc)CH2D, 215-18, ; Bu, ", 160-3, ; ", 4,2,6-DL-EtO2CCH(NHAc)CH2D, 98-100, , ; p-O2NC6H4CH2, 4,2,6-DL-HO2CCH(NHAc)CH2D, 77-100 (182-5)°, +; PhCH2, 4,2,6-HO2CD, 227-9, +; ", 6,2,4-HO2CD, 149-53, +; ", 4,2,6-HO2CCH2D, 196-7.5, -; ", 4,2,6-HO2C(CH2)2D, 162-4; Me, ", 116-19, ; PhCH2, 4,2,6-EtO2CH:CHD, 131-3, ; ", 4,2,6-HO2CCH:CHD, 235-7, ; ", 4,2,6-MeO2CCH:CHD, 122-4, ; Me, 4,2,6-HO2CCH:CHD, 202-4, ; PhCH2, 4,2,6-HO3SD, decomposition, ; ", 4,2,6-H2NSO2D, 205-6, ; ", 4,2,6-EtO2CNH(CH2)2D, 96-7, ; ", 4,2,6-ClH.H2N(CH2)2D, 213-14; p-BzOC6H4CH2, 4,2,6-MeO2CD, 138-40; ", 4,2,6-L-EtO2CCH(NHAc)CH2D, 195-6, 22.220; p-AcOC6H4CH2, 4,2,6-MeO2CD, 103-5; ", 4,2,6-L-EtO2CCH(NHAc)CH2D, 187-9; PhCH2, 4,2,6-(N:CMe.O.CMe:C)CH2D, ; Ph, 4,2,6-HO2C(O2N)2C6H2, 219-22, ; ", 4,2,6-HO2C(H2N)2C6H2, 229-31, ; ", 4,2,6-HO2CD, 230-2, +++; ", 4,2,6-MeO2CD, 148-9, ; ", 4,2,6-BuO2CD, 95-7, ; ", 4,2,6-ClCOD, 100-3, ; ", 4,2,6-Me2N(CH2)2COD, 95-8, +; p-HOC6H4, 4,2,6-HO2CD, , ++; 3,5-Me2C6H3, 4,2,6-MeO2C(O2N)2C6H2, 146-8, ; ", 4,2,6-HO2C(O2N)2C6H2, 216-21; ", 4,2,6-MeO2C(H2N)2C6H2, 163-4, ; ", 4,2,6-MeO2CD, 160-1, ; ", 4,2,6-HO2CD, 265, ++; 3,4-Me2C6H3, 4,2,6-MeO2C(O2N)2C6H2, 125-7, ; ", 4,2,6-HO2C(O2N)2C6H2, 235-40, ; ", 4,2,6-MeO2C(H2N)2C6H2, 123-4, ; ", 4,2,6-MeO2CD, 165-6, ; ", 4,2,6-HO2CD, 267, ; 2-C10H7,

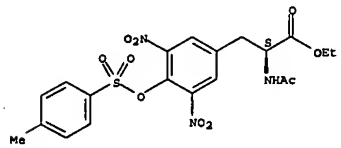
L4 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
4,2,6-HO2C(O2N)2C6H2, 258 (decompn.), ; *, 4,2,6-HO2CD, 260-6, ; 2,4-(O2N)2C6H3, p-EtO2CC6H4, 150-2, ; 2,4-I2C6H3, *, 67-8, ; *, p-HO2CC6H4, 250, ; Ph, 4,2,6-[L-EtO2CCH(NHAc)CH2](O2N)2C6H2, 136-7, 44.922; *, 4,2,6-[L-EtO2CCH(NHAc)CH2](AcNH)2C6H2, 209-9.5, 72.923; *, 4,2,6-L-EtO2CCH(NHAc)CH2D, 106-7, 50.220; ; *, 4,2,6-DL-HO2CCH(NH2)CH2D, 237-8, ; 3,5-Me2C6H3, 4,2,6-[L-EtO2CCH(NHAc)CH2](O2N)2C6H2 , 131-2, 43.122; *, 4,2,6-[L-EtO2CCH(NHAc)CH2](ClH.H2N)2C6H2 , 214-15; *, 4,2,6-[L-EtO2CCH(NHAc)CH2](AcNH)2C6H2, 207, 66.824; *, 4,2,6-L-EtO2CCH(NHAc)CH2D, 158.5-9 , 50.020; *, 4,2,6-DL-HO2CCH(NH2)CH2D, 237-8 (decompn.), ; 3,4-Me2C6H3, 4,2,6-[L-EtO2CCH(NHAc)CH2](O2N)2C6H2, 114.5-15.5 , 44.722; *, 4,2,6-[L-EtO2CCH(NHAc)CH2](AcNH)2C6H2, 190, 7022; *, 4,2,6-[L-EtO2CCH(NHAc)CH2](ClH.H2N)2C6H2, 213-14 (decompn.), ; *, 4,2,6-L-EtO2CCH(NHAc)CH2D, 117-18, 49.520; *, 4,2,6-DL-HO2CCH(NH2)CH2D, 234-5, -; 3,5-MeEtC6H3, 4,2,6-[DL -EtO2CCH(NHAc)CH2](O2N)2C6H2, 118-19, ; *, 4,2,6-DL-HO2CCH(NH2)CH2D, 226-7, -; 3,5,4-I2(HO)C6H2, 4,2,6-(HO2CCH:CH)(O2N)2C6H2, +; *, 4,2,6-[DL-HO2CCH(NH2)CH2](O2N)2C6H2, +; H, 4,2,6-HO2C(CH2)2D, +; *Double, m.p. corresponding alkylphenols; p-BzOC6H4CH2Br, m. 108-11°, and p-AcOC6H4CH2Br, m. 53-6°, by bromination of the p-tolyl esters with N-bromosuccinimide; and DL-N-acetyl[3,5-dinitro-4-(p-tolylsulfonyloxy)phenyl]alanine Et ester, m. 157-8°, from DL-N-acetyl-3,5-dinitrotyrosine Et ester and p-MeC6H4SO2Cl.

IT 903509-20-6P, Alanine, N-acetyl-3-(4-hydroxy-3,5-dinitrophenyl)-, ethyl ester, p-toluenesulfonate
RL: PREP (Preparation)
(preparation of)

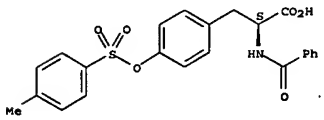
RN 903509-20-6 CAPLUS

CN Alanine, N-acetyl-3-(4-hydroxy-3,5-dinitrophenyl)-, ethyl ester, p-toluenesulfonate (5CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1953:61891 CAPLUS
DOCUMENT NUMBER: 47:61891
ORIGINAL REFERENCE NO.: 47:10502i,10503a-b
TITLE: O-p-Tolylsulfonyl-L-tyrosine and its N-acetyl and N-benzoyl derivatives
AUTHOR(S): Jackson, Ernest L.
CORPORATE SOURCE: Natl. Inst. of Health, Bethesda, MD
SOURCE: Journal of the American Chemical Society (1952), 74, 817-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

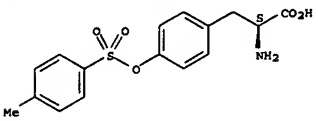
AB L-Tyrosine Me ester (15 g.) with 7.6 g. AcCl in 800 cc. CHCl3, 9 g. anhydrous Na2CO3, and 60 cc. water [Fischer, Ber. 37, 2495(1904)] yielded 91% N-acetyl-L-tyrosine Me ester (I), m. 136-7° (uncor.), [α]D20 29.7° (c 0.41, MeOH); 8.8 g. I and 7.4 g. p-MeC6H4SO2Cl in 185 cc. Me2CO containing 37 cc. N NaOH refluxed 1 hr. and concentrated at 25° to 50 cc. yielded 72% O-p-tolylsulfonyl-N-acetyl-L-tyrosine Me ester (II), m. 90-1° (corrected), [α]D20 15.5° (c 0.8, MeOH). II(5.7 g.) in 100 cc. AcOH and 100 cc. 38% HCl refluxed 2 hrs., diluted with 850 cc. water, and neutralized with NH4OH yielded 4.7 g. O-p-tolylsulfonyl-L-tyrosine (III), m. 213-14° (uncor., decomposition), [α]D20 9° and 9.5°, resp., in N HCl, c 0.42 and 3.16. III (2.3 g.) with 0.7 g. AcCl, 100 cc. CHCl3, 1.2 g. Na2CO3, and 8 cc. water yielded the N-Ac derivative, m. 134-5° (uncor.), [α]D20 29.4° (c 0.83, MeOH); 1.5 g. III, 1.9 g. BzCl, 3 g. NaHCO3, and 40 cc. water yielded 0.9 g. N-Bz derivative, m. 194-5° (uncor.), [α]D20 -1.3° (c 2.61, water containing 1.1 equivs. NaOH).

IT 13504-89-7P, Tyrosine, p-toluenesulfonate (ester)
911670-94-5P, Tyrosine, N-benzoyl-, L-, p-toluenesulfonate
RL: PREP (Preparation)
(preparation of)

RN 13504-89-7 CAPLUS

CN L-Tyrosine, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 911670-94-5 CAPLUS

CN Tyrosine, N-benzoyl-, L-, p-toluenesulfonate (5CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1952:39013 CAPLUS
DOCUMENT NUMBER: 46:39013
ORIGINAL REFERENCE NO.: 46:6591d-i,6592a-d
TITLE: Conversion of optically active α-amino acids into optically active amines with the same carbon skeleton
AUTHOR(S): Karrer, P.; Ehrhardt, K.
CORPORATE SOURCE: Univ. Zurich, Switz.
SOURCE: Helvetica Chimica Acta (1951), 34, 2202-10
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 46:39013

AB DL-PhCH2CH(NH2)CH2OH (I), m. 71.5-3° (cf. Karrer, Portmann, and Suter, C.A. 43, 6979a) (1.5 g.) in 15 cc. absolute C5H5N at 0° was added (1 h.) to 3 g. TsCl (Ts = p-MeC6H4SO2) in 8 cc. C5H5N, the mixture kept 4 h. at room temperature, cooled to 0°, an addnl. 3 g. TsCl in 8 cc. C5H5N, added, the mixture let stand. 1 h. at 0° and 22 h. at room temperature, treated with ice, extracted with ether, the extract washed with 0.5 N HCl and H2O, evaporated, and the residue taken up in C6H6, treated with charcoal, and precipitated with petr. ether to give 59% DL-PhCH2CH(NHTs)CH2OTs (II), m. 102-4°. II (3.5 g.) (original reads MeCH(NHTs)CH2OTs) in 25 cc. C6H6 was added dropwise to 1 g. LiAlH4 in 90 cc. ether (cf. Schmid and Karrer, C.A. 44, 554g), the mixture refluxed 16 h., allowed to remain overnight (protected from H2O), treated with ether, washed with H2O, the layers separated, the precipitate taken up in 10% HCl, the solution extracted 2 times with ether, the combined exts. washed with H2O, dried, concentrated, and the residue crystallized from aqueous MeOH to give 65% DL-PhCH2CH(NHTs)Me (III), m. 55-7° (C anal. 0.76% high). D-I, m. 91.5° (3.35 g.), in 30 cc. C5H5N was added to a cold solution of 11 g. TsCl, the mixture kept 1 h. at 0° and 88 h. at room temperature, and the C5H5N distilled (11 mm., bath temperature 30°), and the residue worked up as above, giving 59% D-II, m. 98-8.5°, [α]D20 50.5° (alc.). D-II (5.95 g.), 1.5 g. LiAlH4, and 160 cc. THF (IIIA) refluxed 23 h. (excess LiAlH4 was destroyed with EtOAc) gave 47% D-III. D-III (1.75 g.) in 150 cc. liquid NH3 and 1.4 g. Na (added in small pieces) were stirred 5 h. in a Dry Ice-alc. bath, 3.5 g. NH4Cl added, and the mixture, allowed to warm to room temperature overnight, diluted with H2O, made acid to Congo red with HCl, extracted with ether (removing p-MeC6H4SH and unchanged material), and to the aqueous solution, concentrated in vacuo to 30 cc., was added anhydrous Na2CO3, the slurry extracted with ether, and the product distilled, giving 0.2 g. impure D-PhCH2CH(NH2)Me, b11 80-90°, [α]D20 28.7° (alc.); picrate, m. 140.5° (from alc.-petr. ether) (picrate of forerun, m. 141-1.5°, mixed m.p. 140°). L-p-HOC6H4CH2CH(NH2)CO2Me (10 g., dried in vacuo over P2O5) in 40 cc. C5H5N was added dropwise to 26.7 g. TsCl in 60 cc. C5H5N at 0°, the mixture kept 60 h. at room temp,. concentrated in vacuo, treated (at 0°) with ice and H2O, and extracted with CHCl3; the extract, washed

L4 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
with 0.5 N HCl and H2O, dried, and concd., gave 92.5% L-p-TsOC6H4CH2CH(NHTs)CO2Me (IV), m. 139° (from C6H6). IV (16.9 g.) refluxed 24 h. with 4 g. LiAlH4 in 190 cc. IIIA gave 81.5% L-p-HOC6H4CH2CH(NHTs)CH2OH (V), m. 178-9°, [α]D20 -48.2° (alc.). V (6.15 g.) and 10.5 g. TsCl in 55 cc. C5H5N kept 1 h. at 0° and 89 h. at room temp. gave 71% L-p-TsOC6H4CH2CH(NHTs)CH2OTs (VI), m. 147-8.5° (from abs. alc.), [α]D17 -33.6° (EtOAc), and a monotosyl deriv., m. 164° (with sintering) (from alc.). VI (3.35 g.) and 1 g. LiAlH4 refluxed 20 h.
in 55 cc. IIIA gave 77% L-p-HOC6H4CH2CH(NHTs)Me (VII), m. 119-20° (from aq. EtOH or MeOH), [α]D19 -21.65°. VII (2.93 g.) with 1.50 cc. liq. NH3 and 2.2 g. Na (6 h. in Dry Ice bath) gave 34% L-p-HOC6H4CH2CH(NH2)Me, m. 110.5-11.5° (from alc.), [α]D17 -52.0° (alc.). L-Prolinol (1.439 g.) and 7.5 g. TsCl kept 1 h. at 0° and 46 h. at room temp. gave 57.5% L-N,O-ditosylprolinol (VIII), m. 104-5° (with sintering at 95-7°) (from alc.), [α]D16 -129.5°. VIII (1.65 g.) refluxed 3 h. with 0.7 g. LiAlH4 in IIIA gave 26% L-1-tosyl-2-methylpyrrolidine (IX), m. 68-9° (from petr. ether), [α]D18 -61.1° (alc.). To 16 g. LiAlH4 in 210 cc. ether was added (15 min., with cooling) 33 g. 5-methyl-2-pyrrolidone in 200 cc. ether, the mixt. refluxed 2.5 h., was treated (30 min.) with enough H2O to destroy the LiAlH4, then with anhyd. Na2SO4, and the org. soln. distd., giving 6.5 g. forerun, b730 86-93° (bath temp. 130°), and 12.8 g. 2-methylpyrrolidine (X), b730 93-6° (bath temp. 160°). X with 22.6 g. tartaric acid gave 65% L-2-methylpyrrolidine acid D-tartrate (XI), m. 127° (sintering at 124°) (from alc.), [α]D21 17.0°. XI (10.7 g.) in 15 cc. H2O at 0° with enough anhyd. Na2CO3 to give a slurry was extd. with ether and the org. product distd., giving 39% L-2-methylpyrrolidine (XII), b728 94°, [α]D22 -11.97° (H2O); picrate, m. 73° (from alc.-C6H6-petr. ether). XII (0.5 g.) with 1.46 g. TsCl in C5H5N kept 1 h. at 0° and 70 h. at room temp. gave IX, m. 70°, mixed m.p. 68-9°, [α]D20 -65.0° (in alc.).

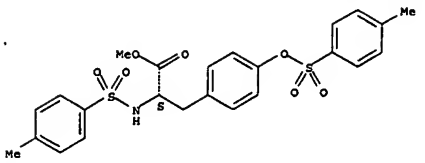
IT 489467-69-8P, Tyrosine, N-p-tolylsulfonyl-, L-, Me ester, p-toluenesulfonate
RL: PREP (Preparation)
(preparation of)

RN 489467-69-8 CAPLUS

CN L-Tyrosine, N-[(4-methylphenyl)sulfonyl]-, methyl ester, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1937:38019 CAPLUS
DOCUMENT NUMBER: 31:38019
ORIGINAL REFERENCE NO.: 31:5324f-h
TITLE: Identification of the amino acids: p-Toluenesulfonyl chloride as a reagent
AUTHOR(S): McChesney, Evan W.; Swann, Wm. Kirk, Jr.
SOURCE: Journal of the American Chemical Society (1937), 59, 1116-18
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 31:38019

AB The following p-toluenesulfonyl derivs. were prepared (the m. ps. reported in the literature are also given, in certain cases marked discrepancies being recorded): dl-alanine, m. 138-9°; d-alanine, m. 132-3°; l-aspartic acid (I), oil; l-cystine (disubstituted), m. 201-3° (decomposition); d-glutamic acid (II), oil; glycine, m. 147°; l-histidine, m. 202-4° (decomposition); l-hydroxyproline, m. 153°; dl-isoleucine, m. 139-40°; d-isoleucine, m. 130-2°; l-leucine, m. 121-2°; dl-methionine, m. 104-5°; dl-norleucine, m. 124°; dl-phenylalanine, m. 134-5°; l-isomer, m. 161°; l-proline (III), oil; dl-serine, m. 212-13° (decomposition); l-tryptophan, oil; l-tyrosine, m. 113-14°; d-valine, m. 147°. The above oils were converted into the Bu esters: I, m. 64-5°; II, m. 61-2°; III, m. 53-5°; dl-lysine, m. 111-13°; the derivative of d-arginine was an oil.

IT 13504-90-0P, Tyrosine, N-p-tolylsulfonyl-, l, p-toluenesulfonate
RL: PREP (Preparation)
(preparation of)

RN 13504-90-0 CAPLUS

CN L-Tyrosine, N-[(4-methylphenyl)sulfonyl]-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.